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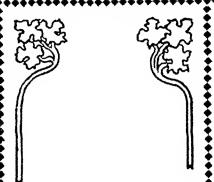
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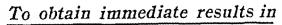
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## AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

FEBRUARY, 1904.

#### GASTROENTEROSTOMY.1

BY JOHN B. DEAVER, M.D., SURGEON-IN-CHIEF, GERMAN HOSPITAL, PHILADELPHIA.

Gastroenterostomy at the present day has a definite position in surgery, with a constantly widening of its field of usefulness in the treatment of lesions of the stomach or duodenum.

Twenty-two years ago Wolffler performed the first operation upon a patient where pylorectomy was impossible, and in 1900 Mayo Robson tabulated 1978 cases reported. At the present time gastroenterostomy is performed many times as a routine procedure in certain gastric diseases without much more comment than a cholecystostomy for a diseased gall-bladder.

During these twenty years, however, while the indications for the operation have become more definite, the method of operating and the technique of operation have been the subject of spirited debate. To overcome the confliction of the direction of peristalsis was the first important step, and many modifications in the original operation were made.

Gastroenterostomy was performed at first for the relief of the starvation in obstructive carcinoma of the pylorus, and then, as has happened so often in surgery, a palliative measure was broadened in scope until it became a valuable method of treatment. The one great indication for gastroenterostomy is found in all lesions of the stomach where the contents of the latter are not evacuated. Whether this is due to a malignant or benign obstruc-

<sup>&</sup>lt;sup>1</sup> Read by title before the Southern Surgical and Gynecological Association, Atlanta, Ga., December, 1903.

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tion, an inflamed or ulcerated pylorus, or atony of the gastric muscle, the retained stomach contents must be provided for by an anas-

tomotic opening.

When carcinoma of the pylorus has progressed so far that its removal is impossible, the last months of the patient may be made more restful by the cessation of vomiting and the ability to assimilate food. In obstruction of benign origin usually consequent upon the healing of an ulcerated area of the pyloric mucous membrane, pyloroplasty is sometimes combined with gastroenterostomy, especially in those cases where a gastric pouch has formed, with loss of the muscle power of the stomach. Where the latter complications do not exist gastroenterostomy is not required, and if performed, soon loses its intended purposes and merely aids in the formation of adhesions.

Bleeding from acute or chronic ulceration of the wall of the stomach frequently offers a positive indication for gastroenterostomy, in order to place the mucous membrane in the region of the pylorus, the most frequent site of ulceration, in a state of partial rest, at least. In acute ulcers the excision of the bleeding point would seem to be the ideal operation, but the consensus of opinion of those of large experience in this work favors a simple gastroenterostomy.

A gastroenterostomy with correct technique will keep the stomach empty, and with the aid of careful feeding sufficient rest can be

obtained to enable the ulcerated area to heal.

When a considerable area of mucous membrane surrounding an ulcer is the seat of marked inflammation, or in large erosions or in multiple ulcer direct treatment cannot be done, gastroenterostomy offers by far the best method of procedure. A chronic ulcer, especially in the neighborhood of the pylorus, requires the exercise of great discrimination as to whether a pylorectomy is necessary.

The literature of instances where malignant disease has developed upon the site of a chronic ulcer is increasing rapidly, and such a termination must always be considered and its likelihood an indication for the excision of the pylorus. Gastroenterostomy is too often considered a last resort for a carcinoma of the pylorus causing obstruction, whereas the lesion should have had surgical interference at a time when a cure was possible. But, on the other hand, it must be admitted that in many cases believed at the time of operation to be malignant by reason of enlarged inflammatory lymph nodes, induration about the ulcer, etc., gastroenterostomy has cured the condition and disproved its malignancy.

The various contractions consequent upon chronic gastric or duodenal ulceration may obstruct the stomach and require gastroenterostomy. In hour-glass stomach it is preferable to divide the wall of the organ in the long axis and close in the opposite direction, but when this is deemed inadvisable gastroenterostomy may be performed. In those cases of hour-glass stomach when the constriction is near the middle, and two large pouches are formed, a gastrogastrostomy at the most dependent portion of the pouches gives better results than gastroenterostomy.

In cases of extensive dilatation of the stomach with loss of motor power consequent upon a strictured duodenum, the result of ulcer. the anastomotic opening is required. The stomach lessens in size to an extent which will depend entirely upon the contractile power of the muscular coat. When the condition of dilatation has lasted for a long time and has appeared gradually, it is questionable whether there will be any actual lessening in the size of the stomach after operation; but if dilatation has come on very rapidly it will be readily seen that the muscular tone has not been overtaxed, and. therefore, the organ should regain its normal size in a comparatively short time. I would lay stress upon the careful examination of cases of dilated stomach. In some instances this condition is caused by kinking of the pylorus from the downward displacement of the organ due to peritoneal relaxation. In gastroptosis with dilatation of the stomach better results are obtained, in my opinion, by a gastroplication and a gastroenterostomy than by the other methods sometimes used.

In some cases of fistulæ between the biliary tract and the stomach where the extent and density of the adhesions may prevent the separation of such adhesions and the repair of the fistula with safety, gastroenterostomy gives good results. Even where gastrolysis can be performed and the fistula closed, the rest and drainage which gastroenterostomy affords gives additional security to the perfect healing of the stomach. In addition, adhesions are likely to reform, and in such an event the artificial opening prevents the dilatation and other symptoms incident to pyloric narrowing.

In those intractable cases of chronic gastritis where multiple erosions of the stomach are present at the pyloric region, with the mucosa in the neighborhood of the erosion deeply hemorrhagic, and with the occasional "occurrence of profuse or even fatal hemorrhage" (Osler), gastroenterostomy, by placing the pylorus at rest,

may cure the condition.

Å secretory neurosis of the stomach, with hypersecretion of hydrochloric acid, known in Germany and France as "Reichman's disease," is frequently rebellious to internal medication. In this disease, while the irritation of the highly acid gastric juice induces pyloric spasm at first, yet in most instances atony and dilatation of the stomach occur, and the pylorus becomes eroded and fissured. In these cases gastroenterostomy places the organ at rest and prevents the accumulation of the intensely acid gastric juice with its severe symptoms.

Mayo Robson suggests that, in acute dilatation of the stomach, after lavage has failed, the abdomen should be opened, the stomach emptied and connected with the jejunum, and Weir advises the

same operation in tetany, which is often associated with a dilated stomach and may be caused by it.

The methods most often used at the present time for performing gastroenterostomy are: (1) the anterior operation; (2) the posterior operation, through the transverse mesocolon; (3) opening the gastrocolic omentum above the colon and anastomosing the jejunum to the posterior wall of the stomach; (4) the Roux Y operation, a modification of Wolffler's second method; (5) Kocher's operation.

The anterior operation is now usually performed by bringing the jejunum, not the duodenum, up over the great omentum and transverse colon and suturing to the stomach near its dependent portion. While in the hands of some good results are obtained, yet I believe that it entails greater risk from adhesions and intestinal obstruction than is the case in the posterior operation. Another objection is that the site of anastomosis is made too far above the greater curvature and not at the most dependent portion of the stomach, so essential where the stomach no longer possesses much muscular power. care is taken, however, the anterior opening can be made nearly as low as the posterior, and, at any rate, it is usually believed that the traction of the small bowel brings the anastomosis to the lowest level, finally. After performing the gastroenterostomy the proximal and distal ends of the loop of the small bowel should be stitched to the stomach, the former at a point higher and the latter at a point lower than the anastomotic opening, preventing, to a great extent, any tendency toward spur formation.

The posterior operation is performed by making an incision in the transverse mesocolon, vertical in direction, to avoid interference with the blood supply of the colon, through which the posterior wall of the stomach is delivered and to which the jejunum is to be attached. The jejunum can always be readily found by passing the hand behind the coils of bowel to the left side of the second lumbar vertebra, where the duodenojejunal junction is grasped. I make it the rule to allow free play of the jejunum by leaving sixteen to eighteen inches of bowel between the anastomosis and the junction with the duodenum. This is done for several reasons: it prevents any kinking of the ligament of Treit, tends to prevent spur formation, and, most important of all, if any subsequent procedures are to be employed, such as enteroenterostomy or Roux's operation, sufficient bowel is left for such operations.

In incising the stomach, as well as the intestine; the incision should first be carried down to the mucous coat, which will then protrude, when, with a pair of tissue forceps, it is grasped and separated at the margin of the wound for some distance from the submucous coat (Robson and Moynihan). The mucous membrane is then cut away to the extent of the length of the wound and about one-half to three-quarters of an inch in width. This prevents the

mucous membrane from pouting into the anastomotic opening and lessening its size, which might interfere during the repair of the wound with the emptying of the stomach, unless the opening is made liberally large. To prevent the slipping of a knuckle of bowel between the margin of the opening made in the transverse mesocolon and the wall of the stomach and consequent intestinal obstruction, as well as to prevent the circular compression of the afferent and efferent loops of the jejunum close to the anastomosis, the margins of the opening made in the transverse mesocolon should be stitched to the stomach wall at one or more points and about one inch away from the anastomotic opening.

The supracolic method merely consists of opening the gastrocolic omentum by a vertical incision, bringing up the jejunum over the omentum and transverse colon and suturing to the posterior wall of the stomach. It has no advantages over the anterior operation

and is exposed to the same risk of adhesion formation.

Roux advocates an operation which seems to offer many advantages. The jejunum is divided, 20 to 40 cm. (eight to sixteen inches) below the point where it passed beneath the transverse colon and the distal end implanted into the stomach, the proximal end being sutured into an opening made in the descending limb, which has been sutured to the stomach and about four inches below the latter. It can readily be seen that the "vicious circle" cannot occur, as the bile and pancreatic secretion by the force of gravity will not return to the stomach, unless there is regurgitation of the intestinal contents. The objection that has been raised to this operation is the small opening afforded from the stomach by the rather narrow diameter of the jejunum. Such opening is not smaller, however, than that obtained by the use of the Murphy button or Mayo Robson bobbin, and not any less than the normal pyloric orifice. I have performed the operation without any disagreeable sequelæ at all, but as I have had like results from the same number of anterior and posterior anastomosis, I have not been able to draw any deductions regarding its greater value than the other operations. Roux's method requires some judgment in its use, and, unless performed with great care, subjects the patient to more risk than the simple posterior operation. Roux indicates its use in benign stenosis, gastroptosis, and gastrectasis. As will be seen later, the operation is of great value when the vicious circle has already occurred.

Kocher endeavors to avoid the return of intestinal contents into the stomach and their resulting decomposition and absorption by bringing the jejunum vertically upward, incising it at right angles to its long axis and suturing to the stomach, so "that the proximal portion of the loop passes vertically upward and the distal portion vertically downward, the former opposite to the stomach. A flap is also formed from the intestine to prevent regurgitation into the stomach." I do not believe, however, that the valve persists for

any length of time, nor does the operation prevent the overfilling of the duodenum any better than the posterior operation.

In all of these operations various mechanical devices are used to perfect the anastomosis, of which the Murphy button is, doubtless, the most popular. Personally, I use simply a needle and thread, though in certain cases I have used both the Murphy button and the Mayo Robson bone bobbin. The great advantage of the needle-and-thread operation is that the materials are always at hand, the opening can be made of any length, thus lessening the tendency to subsequent contraction, which may close the opening. The objections to the mechanical devices are the rather small opening allowed and the subsequent contraction of the opening, particularly when the Murphy button or Senn's plates have been used. If too large a button or bobbin has been used, pressure necrosis of the bowel and perforative peritonitis may result.

Of the various other methods of performing the anastomosis, I have had no experience. I do not use the elastic ligature, because I see no advantages to be derived from its use, and it has the objection that we can never be absolutely sure that the ligature will cut through and establish the opening. The Connell suture has also been recommended, but I have never used it, nor do I use the clamps for the stomach and intestinc. By the proper disposition of gauze the portion of bowel to be anastomosed, brought out of the abdomen, can be so compressed against the margin of the abdominal wound that no escape of contents occurs when it is opened. There is no danger of bleeding if the coats are well sutured, and if such is feared, Down's instrument could be used in making the openings. Personally, I do not use the cautery knife, believing it to be cumbersome and tending to a needless multiplicity of instruments.

The prevention of vomiting after operation from the formation of the vicious circle has occasioned much thought upon the part of many surgeons. Some deny that they have ever had to deal with this distressing complication, and it is fortunate that this vomiting is not frequently met with; yet that it does occur, even with perfect technique, cannot be disputed. The term vomiting from the vicious circle is applied to that condition where the gastric contents pass into the proximal or afferent limb of the loop, become mixed with the bile and pancreatic secretion and are returned to the stomach. Reflux vomiting (Fowler) is due to the passage of the secretions alone into the stomach, through the new opening, or backward through the partially permeable pylorus. The cause of such severe vomiting has not been determined, some observers having shown that the secretions of the liver and of the pancreas can be led directly into the stomach without impairing digestion or causing vomiting. Fowler believes that the symptoms arising from the vicious circle are due either to "the passage of food into the duodenum and its more or less prompt reflux into the stomach, followed by its injection by vomiting, or from distention of the duodenum and a relative stagnation of the stomach contents from motor insufficiency." To correct these conditions after performing the usual posterior anastomosis, Fowler performs enteroenterostomy between the afferent and efferent portion of the loop of jejunum, and, finally, passes a No. 20 silver wire two or three times around the afferent loop between the two points of anastomosis and drawing upon the turns tightly enough to occlude the lumen of the intestine without strangulating its wall. This absolutely prevents the duodenal end of the loop from communicating directly with the stomach.

The question as to whether the enteroanastomosis should be performed in every case must be answered in the negative. I formerly used such a procedure, but at the present time believe that the simple posterior gastrojejunostomy is more rapid, safer, and perfectly efficacious in the great majority of cases, reserving subsequent operative procedures in the event of the establishment of severe

vomiting.

The following case illustrates the few points that I particularly

wish to emphasize:

Miss M. J., aged twenty-four years, was admitted to the German Hospital on July 7, 1903. Her family and previous personal history presented nothing of interest, nor did her occupation, that of tobacco

stripper, have any influence on her condition.

Three years before the first symptoms of gastric trouble appeared with a gradual failing of the appetite, eructations of gas and fulness and distress after taking food. A year later she began to vomit after eating. The vomited material was quite sour, the sourness increasing when the food was retained for a while before the vomiting. There was never any hematemesis. The gastric distress increased and was soon accompanied by a burning pain in the epigastrium, just above the umbilicus, and referred along the costal margins of both sides. This pain was not relieved by eating or drinking. The bowels, which had been regular during the earlier months, became constipated. There was never any diarrhœa.

Her treatment had consisted, after a course of the various stomachies, of lavage practised every alternate day since December, 1902. When the stomach washing was practised in the morning remains of food eaten the night before were found, together with much

mucus.

Upon admission nothing of moment was observed by a physical examination. There was tenderness of the abdomen 1 cm. above the umbilicus and over an area 3 cm. in diameter, and also a tender point over the twelfth rib, posteriorly. The stomach capacity was 1500 c.c., the lower border reaching to 1 cm. above the umbilicus when distended.

Operation, July 8, 1903, under ether anæsthesia. An incision five inches long was made through the right reetus, the peritoneum was opened and the stomach appeared immediately below the wound. Numerous adhesions, fibrinous in character, were found around the neek of the gall-bladder and duodenum. The gall-bladder was normal and slightly distended. The stomach was then carefully examined and observed to be slightly enlarged, rather low in position, and the pyloric opening somewhat thickened, otherwise negative.

The intestines were walled off with gauze pads, the transverse eolon and mesocolon delivered out of the wound and protected with gauze. The transverse mesocolon was ineised and the posterior surface of the stomach exposed and brought out of the wound; a loop of the upper portion of the jejunum was delivered and brought up to the posterior wall of the stomach, to which it was stitched by a continuous Lembert suture, introduced for a distance of about two and a half inches. An incision was then made into the jejunum, about two inches in length, through the serous and muscular coats, and the protruding mucous membrane excised. A similar procedure was performed upon the stomach. The free edges of the stomach and jejunal wounds were united with through-and-through silk suture. The Lembert suture was then continued anteriorly, completing the peritoneal apposition. The abdomen was closed with tier suture.

The patient reacted well from the operation, was free from vomiting until July 13th, when 700 e.c. of dark-green bile was vomited.

General condition good.

July 15th. Patient vomited bile during the night. Appetite good; feels better than she has in years. Stitehes removed. Incision healed by first intention.

17th. Patient vomited bile, with small portion of feeal matter.

18th. During the early morning the patient vomited; vomitus stercoraceous in character, about 300 e.e., and an intestinal obstruction was believed to have taken place, necessitating a second operation.

When the abdomen was opened the omentum was found adherent to the old sear. These were separated, and the omentum and transverse colon turned upward. This reflection upward carried several eoils of small bowel along, and it was found that the proximal and distal limbs of the anastomosed loop were firmly adherent to the posterior layer of the transverse mesoeolon, interfering to a marked degree with the peristalsis of the bowel. The adhesions were all separated and such bowel surfaces as were denuded by the separation were sutured with silk or covered with eargile. The gastroenterostomy was apparently perfect. An enteroenterostomy was then performed, 15 cm. (six inches) below the anastomotic opening, in the usual manner. The abdomen was closed by tier sutures. There was some vomiting of a green material upon the two days following operation, which stopped upon the use of lavage.

25th. Stitches removed; wound healed by first intention.

26th. Patient vomited twice about 300 c.c. of light-greenish material. Wine of ipecac, 10 drops every hour, was given.

27th. No vomiting. 31st. Ipecac stopped.

August 2d. Vomited 300 c.c. of light-green material about 10 P.M. Vomiting cannot be attributed to anything eaten. Placed upon ipecac wine 10 drops every two hours during the day.

7th. Vomited small quantity of yellow material. Ipecac stopped. 12th. Discharged; condition fine. Is gaining weight, and has not

vomited since August 7th.

On September 14, 1903, this patient was readmitted to the German Hospital. She stated that on August 16th, four days after her discharge, vomiting had recommenced, at first of bile and later of food and bile. When admitted she vomited everything given by the mouth, and large quantities of thick, ropy, dark-green material, with a very strong odor. Feeding by rectum was begun, but notwithstanding this, the patient continued to vomit the thick, dark-green material, containing large quantities of bile. On washing out the stomach large quantities of the same material were obtained. It was evident that the biliary and pancreatic secretion were regurgitating into the stomach and causing the vomiting.

Her nourishment was good, notwithstanding the vomiting, proving that the food must be digested in great part, especially as the patient does not seem to have lost much weight. Eyes examined by Dr. W. T. Shoemaker, with no abnormal findings. By a rectal examination the pelvic organs were apparently normal; there were

no symptoms or signs of locomotor ataxia.

Operation was performed on September 19th. When the peritoneum was opened the omentum was found universally adherent and there were dense adhesions between the coils of bowel. gastroenterostomy was exposed and the opening found to be freely The enteroenterostomy was exposed, some difficulty being encountered in distinguishing the parts of the anastomosis by reason of the numerous adhesions. When these were separated the anastomosis was found to be in perfect condition, with some sacculation. Adhesions were further separated throughout the abdominal cavity. The entire omentum was ligated and cut away. The gall-bladder was found normal in size, numerous adhesions found around it; stomach normal in size. By means of a pedicle needle a piece of silver wire was passed around the pylorus and tied. Parts were then returned. Abdominal cavity filled with normal salt solution and the abdomen closed by tier suture. The patient was shocked, the pulse barely perceptible at the close of operation. An intravenous injection of salt solution was given before leaving the operating room.

September 20th. Patient has vomited bile several times during the

day.

22d. Buttermilk ordered. Patient feels somewhat distressed in the epigastric region. No vomiting.

23d. Patient feels well; no epigastric distress. 29th. Ate light diet. No nausea or distress.

October 10th. Patient vomited after breakfast.

11th to 15th. Vomited several times each day; complained of abdominal pain; there was some tympanites. The fourth operation was, therefore, performed, and a coil of small intestine found closely adherent to the parietal peritoneum. The intestines were found universally adherent to each other and to the remains of the omentum, binding together the transverse, ascending, and descending colon and sigmoid flexures and various loops of small intestine, one to another. No portion of the bowel, excepting about five feet of ileum, was free from adhesions. The adhesions were separated, bleeding points ligated, and all denuded surface covered with cargile. The entercenterostomy and gastroenterostomy were examined and found patulous. At no portion were the intestines collapsed or unduly distended. The abdomen was closed by through-andthrough sutures of silkworm gut.

17th. Much vomiting. 19th. No vomiting.

Stitches removed; wound healed without inflammation.

November 2d. Patient allowed to sit up in a chair; no vomiting; feels strong.

9th. Patient walking about.

Discharged.

The patient was home for ten days, when she again began to vomit as before, in the morning bile, later in the day particles of food; would vomit two or three times every day.

On readmission the patient's nutrition is good. On abdomen two scars of former operations; slight distention of the stomach.

The fifth operation was performed December 7, 1903. incision seven inches long was made dissecting out the last cicatrix, peritoneum opened, and many adhesions found between intestines and under-surface of incision. Universal adhesions were present throughout the intestinal canal; these were carefully dissected free and two holes in the intestine, which were accidentally made, were closed by sutures of silk. Abdomen was filled with salt solution and the wound closed by through-and-through sutures of silkworm gut.

January 19, 1904. Patient apparently entirely well.

This unfortunate woman has, therefore, undergone five operations, one after the other, for the relief of severe vomiting. enteroenterostomy and occlusion of the pylorus have both failed to relieve her condition. The etherization in each operation has been easy of accomplishment. Every cause for vicious circle or for jejunal reflux seems to have been eliminated, except the influence of adhesions, which have been met at each operation. The patient gained in weight, even while vomiting, indicating that the digestive

power was unimpaired.

From this case and two former ones requiring reoperation I must believe that the formation of adhesions plays the chief part in favoring severe vomiting, by the inhibition of the normal peristalsis and the retention of the bile and pancreatic secretions in the loop of the afferent limb of the jejunum. This limb must be a loop, as we cannot make a rigid tube from the duodenum to the enteroanastomosis, and in the absence of sufficient muscular tone or the presence of obstructing adhesions the secretions must accumulate. The effect of food, the exciting agent of the flow of these secretions, causing vomiting an hour or so after eating, also would seem to indicate the influence of retained secretions. The sagging of the jejunum from the weight of the secretions dragging upon the efferent loop may also have an influence upon the stomach.

My future procedure will be to perform the posterior method of anastomosis or the Roux Y operation, and in the event of vomiting following the former method I will reoperate, divide the afferent limb just below the stomach, and implant it, as in the Roux Y, into the efferent limb some 10 or 15 cm. (four or six inches) below the stomach, closing the shallow sac above close to the anastomotic

opening.

The after-treatment of a patient upon whom gastroenterostomy has been performed is of the greatest importance. Shock, vomiting, and pneumonia should be guarded against at the time of operating. I use a hot-water bed, hot bottles, and a cotton jacket during the operation, and have the anæsthetic administered with the greatest care. The arms should never be folded across the chest, thereby impeding respiration.

If shock occurs the usual remedies are administered, and, above all, saline solution by the bowel, at first combined with whiskey, and later intravenously, if the condition of the patient should demand it.

Vomiting is greatly to be feared, and while I usually allow liquid food eighteen hours after the operation, the occurrence of nausea is an indication for its discontinuance, substituting rectal feeding. If vomiting does occur, the best treatment is, undoubtedly, gastric lavage, using small quantities of water at a time, 200 to 300 c.c., and giving absolutely nothing by the mouth.

Peritonitis is unavoidable if the anastomosis gives way, but by the careful use of the needle-and-thread method the danger is minimized and far less liable to happen than with the use of mechanical appliances. Upon the onset of peritonitis, a reoperation is imperatively demanded, the anastomosis strengthened, and the peritoneum washed out. If the shock does not prove fatal, such a patient should usually recover, as the infection from the fasting stomach is not of a very virulent type.

#### THE NERVOUS COMPLICATIONS AND SEQUELÆ OF SMALLPOX.\*

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SMALLPOX, like other infectious diseases, may present various nervous complications and sequelæ. Indeed, almost the first effect of the variolous poison is observed in the violent frontal headache. which constantly is an early symptom. Sharply contrasted with the many other complications and sequelæ of variola, the affections of the nervous system are not strictly confined to certain stages of the disease itself, not necessarily immediately sequential, nor are they at all related to the severity of the infection. It seems that the variolous process possesses, in a marked degree, the power to awaken latent predispositions to nervous disease, as well as to independently disorder function and create anatomical alterations in the various nervous structures of the body. These affections may be gross anatomical, purely functional, or both. Many cases present a varied clinical picture, which leaves us in doubt as to the exact nature of the lesion, and until further post-morten examinations and other investigations have bettered our present knowledge, we must be content with collecting the rare and interesting cases for the literature and for future investigations and diagnosis. These complications and sequelæ invade all possible provinces of the nervous system—the brain, spinal cord, and peripheral nerves. Truly, the nervous complications and sequelæ of this loathsome disease offer a most fruitful and little-worked field for research.

Convulsions are often seen in children, and usually precede the eruption. They are mentioned by Troussean, who endorses the belief of Sydenham, that they possess diagnostic value, especially in the young. Sydenham states that convulsions occur more frequently in smallpox than in any of the xanthematous diseases.

Smallpox often exerts a profound effect upon the pysche.

In order of frequency, as a cause of the febrile deliria and psychoses, smallpox is placed sixth by Berkley. Kraeplin, who is, perhaps, the greatest authority upon this subject, also places variola in the same causative relation.

We may recognize at least four types:

- 1. Initial delirium.
- 2. Febrilc delirium.

<sup>\*</sup> Read before the Clinical and Pathological Section of the Cleveland Academy of Medicine, October 2, 1903,

- 3. Collapse or exhaustion delirium.
- 4. True postvariolous insanity.

The occurrence of initial delirium is quite constant, usually appearing toward the evening of the second or third day; the mind wanders, the speech becomes incoherent, and a true confusional condition develops. Throughout the attack there is much sleeplessness and great disquietude. This delirium differs entirely from that with specifically colored delusions and accompanied by tremors, the delirium alcoholicum, which commonly occurs in inebriates attacked by smallpox.

Seppilli and Maragliano<sup>6</sup> reported three cases of acute mania occurring in smallpox. Two recovered and one remained incurably insane. Trousseau<sup>7</sup> referred to the case of a woman who was seized with an acute mania during the progress of a mild attack of smallpox. She had never before shown any symptoms of mental disturbance. Corlett<sup>8</sup> records the occurrence of an acute mania in the course of a discrete smallpox. The sufferer remained violently

insane for six days, when death came.

Grave changes in the mental state, with peculiar speech disturbances, have been observed to follow variola by Welch, Westphal, Otto, Toville, Zaccoud, Riva, Quinquaud, Leudet, Whipham and Myers, Pforzheim, Béhier and Lionville, Long, the writer, and others. These mental changes seem to be a part of widespread changes in the nervous system, and yet sufficiently uniform in their symptom groups and their pathological pictures to deserve separate and detailed description, which will be given later, in connection with two personally observed cases.

The occurrence of true dementia paralytica has been observed to follow variola by Mabille<sup>22</sup> and others. In fact, the writings of Hoppe,<sup>23</sup> Lagardelle,<sup>24</sup> Berthier,<sup>25</sup> Kiernan,<sup>26</sup> and many lesser known observers show that smallpox is a fruitful cause of mental alienation.

Meningitis, fortunately, is a rare complication. It is usually purulent, and probably a metastasis from the skin lesions. Gregory<sup>27</sup> states that it is most liable to occur in children and during the period of suppuration and beginning desiccation.

Reiner<sup>28</sup> has recorded a severe meningitis of the convexity occur-

ring as a variolous complication.

The occurrence of paralysis in smallpox has been commented upon since that exanthem's history passed from tradition to record. Indeed, literature bears out the statement of Landouzy, that "of all the eruptive fevers smallpox is, without contradiction, the one in which paralysis most frequently occurs, either at the onset, in the course of, or at the decline." How frequently it occurs, unfortunately, we have no means of ascertaining. That smallpox is less liable to cause the complication than typhoid fever seems to be the opinion of Landouzy, but from a limited personal observation and an extensive search of the literature, I question the statement.

The nature, origin, and seat of the various paralytic affections attending and consequent to variola are so varied that classification is most difficult. That they may originate in the brain, spinal cord, or peripheral nerves is certain. It is also positive that we may have a combination of two or more of these forms.

Paralysis may occur at the very onset of the infection, at any time

during its course, or at any period of convalescence.

The majority of the paralytic affections arc, as in other acute infections, of neuritic origin. Landouzy<sup>31</sup> believed that paraplegia was most frequent. I believe, however, that he included the cases of brachial paraplegia, as well as the crural monoplegias, in his consideration. Rejecting these as most likely peripheral neuritides, we place paraplegia of spinal origin farther down in the list of nervous complications and sequelæ of variola.

All are agreed upon the rather fortunate outcome of most of the

paralyses of variola.

E. Wagner<sup>32</sup> has observed, on post-mortem examination, evidences of localized non-purulent encephalic disease. And that we may have a non-purulent meningoencephalitis of a simple character complicating variola, I believe, the first case to be reported in this paper will fully demonstrate.

Areas of simple softening and blood extravasations may occur in the brain and produce aphasia, monoplegia, or hemiplegia. According to Immermann,<sup>33</sup> such lesions may remain latent throughout life

and be discovered only at autopsy.

Reiner,<sup>34</sup> Landouzy,<sup>35</sup> Edes,<sup>36</sup> Osler,<sup>37</sup> and many other writers mention and some relate personally observed variolous hemiplegias, but if the meagreness of the literature is an index of their infrequency,

then they are rare, indeed.

Clinicians have long been aware of the relative frequency of cord affections in variola. The severity of the infection appears to have little to do with their occurrence, since they appear to develop with equal frequency in varioloid. The observed cases have been usually paraplegia, of the motor type, developing in any stage of the disease from the prodromal to a far-reaching period of convalescence. Leroy d'Etiolles<sup>38</sup> has recorded the occurrence of such affections in the stage of incubation before the proper beginning of the variola.

Trousseau<sup>so</sup> observed in cases where severe lumbar pain was complained of in the initial stage that a slight degree of paraplegia was often present. It was manifested by subjective numbness, tenderness, and loss of power. Occasionally the bladder was involved, producing difficult micturition and occasional retention. These symptoms usually disappeared with the appearance of the eruption, but in rare cases remained to the middle of the second week.

Henderson, 40 Westphal, 41 Kahler and Pick, 42 and others state that rarely acute ataxias have been observed to follow variola. It is quite probable that these cases of ataxia are ataxic forms of neuritis,

although many of the cases of pseudomultiple scleroses manifested some ataxia. Henderson's<sup>43</sup> case of postvariolous ataxia presented numbness and tingling of the legs and hands. The skin reflexes and deep tendon reactions were all absent. The patient later recovered his power and station. In the discussion which followed Dr. Henderson's report, Dr. Whipham<sup>44</sup> referred to two similar cases, which, I presume, are embraced in the report of Whipham and Myers.<sup>45</sup> These cases have been looked upon as pseudotabes, the so-called ataxia variolique, but more likely belong to a class of disseminated focal inflammations scattered throughout the brain and spinal cord.

Peter Marie,<sup>46</sup> Sottas,<sup>47</sup> Long,<sup>48</sup> Charcot,<sup>49</sup> and others have observed typical examples of disseminated sclerosis following smallpox. The case of Sottas is quite typical, but it appears from the reports of most of these cases that, while for a time they presented an array of symptoms much like true disseminated sclerosis, they later slowly grew better, thus making a marked departure from the ordinarily progressive course of that disease.

Enough knowledge of the pathological changes has been found at the root of the disorder to demonstrate that we have disseminated encephalomyclitis which, although followed by a sequential sclerosis, has little or no tendency to extend or multiply itself. This subject

will again be adverted to.

Westphal<sup>50</sup> recorded a case which was followed by paralysis of the legs and bladder that was due to disseminated foci of inflammation involving the gray and white matter of the spinal cord. Foci of softening in the structures of the cord have been described by Damaschino<sup>51</sup> and Joffroy,<sup>52</sup> Hayem<sup>53</sup> and Landouzy.<sup>54</sup>

Fiessinger<sup>55</sup> remarked the occurrence of acute myelitis appearing

as a complication and disappearing with the disease.

Steven Mackenzie<sup>56</sup> has reported a case of poliomyelitis anterior as a sequel of variola. Damaschino and Roger<sup>57</sup> and Landouzy<sup>58</sup> record acute monoplegias in children presenting the clinical picture of acute inflammation of the cells of the anterior horns of the cord.

Although Huchard<sup>50</sup> observed not more than ten paraplegias in 2000 patients affected by smallpox, yet Landouzy<sup>60</sup> states that para-

plegia is the most frequent form of variolous palsy.

A rapidly ascending myelitis presenting clinical symptoms of Landry's paralysis has been recorded by a number of authors: Marinesco and Oettinger, <sup>61</sup> Gubler, <sup>62</sup> Leyden, <sup>63</sup> Gros, <sup>64</sup> Chalvet, <sup>65</sup> Marie, <sup>60</sup> Bernhardt, <sup>67</sup> Gros and Beauvais. <sup>68</sup> These cases, as a rule, are rapidly fatal.

F. W. Goss<sup>69</sup> observed a typical case of acute ascending paralysis occurring early in a mild varioloid. It proved so quickly fatal that

the patient died four days after the first paralytic symptoms.

Dr. M. Friedrich<sup>70</sup> personally related to me the details of a rapidly fatal case of undoubted ascending or Landry's paralysis, appearing

in the stage of desquamation in a comparatively mild case of small-

pox during our late epidemic in Cleveland.

It would appear from Oettinger and Marinesco<sup>71</sup> that the pathological picture of Landry's paralysis may exist in variola in combination with the disseminated myelitis described by Westphal. Indeed, a recent communication appears to have firmly established this fact.

Cases have been described by Vulpian<sup>72</sup> and others of acute ascending paralysis from variola in which a most careful search failed to show a myelitis. It seems reasonable to believe that these

cases are polyneuritic in origin.

A careful examination of the literature convinces me that we have occurring as a complication or sequel of smallpox a disseminated encephalomyelitis, which possesses clinical features and pathological changes clearly entitling it to be recognized as a clinical entity, and which occurs with sufficient frequency to demand our special consideration and study. It occurs in other infectious diseases, as the case reported by Ebstein's conclusively proves. Ebstein's case is quoted particularly because it complicated typhoid fever and the symptom-complex was identical with that of the variolous cases, and the post-mortem disclosures were more complete and in keeping with the clinical findings.

I believe that these cases have in time past been described as and believed to be the disease which was named by Charcot disseminated sclerosis. Some of the reported cases bear a very close resemblance, but the majority are but coarse imitations. In this connection it is not thought wise to discuss the pros and cons of the question, but

to report two personal observations.

I have been able to find fifteen cases in the literature, all presenting:

1. More or less ataxia in the four extremities, usually most marked

in the legs.

2. Slowness and awkwardness of movement.

3. Slow, monotonous, explosive manner of speaking.

4. Faulty articulation.

5. A varying degree of mental degradation.

6. A decided tendency toward recovery.

The following personal observations are added to the literature: To the courtesy of Dr. Martin Friedrich I am indebted for the

privilege of examining and reporting this case:

CASE I.—E. L., male, white, aged thirteen years, was normally born in the United States, and of German parents. He had never suffered any severe illness and was considered a large, well-developed boy. His father and mother are strong, healthy people, each giving a good family history. There are four other children in the family, all of whom are well. There have been no deaths in the family, nor history of miscarriages or stillbirths.

Edward was taken sick the last of June, 1902. The family attend-

ant, Dr. Christian Sihler, was called and found the boy's temperature to be 103° F., from which it shortly rose to 104.5° F. Nothing could be found to account for the temperature, and because of numerous cases in the neighborhood, smallpox was suspected. On the fourth day an eruption appeared, and Dr. Martin Friedrich was called in consultation and made the diagnosis of discrete smallpox.

The temperature immediately fell on the development of the eruption, but little secondary fever developed, and the boy was not thought to be very ill. There had been no convulsions or other disturbances of the nervous system, either in the prodromal period or immediately following the eruption. He was sent to the Detention Hospital, where, for the first ten days, he was at no time confined to bed. He ate well, slept well, and did not complain. During the first week in the hospital an abscess developed on the right leg, which, although quite large, caused him little discomfort. He was homesick and anxious to go home, but was put off from time to time and felt very badly about the delay. On July 15th, and on the thirteenth day of his residence in the hospital, his father came to take him home, when the boy was discovered lying on the bed in a stupid condition and could not be aroused. It was thought, perhaps, that he was soundly sleeping, and the father went home without him. The attendant, failing to arouse the boy, informed Dr. Friedrich of his condition, who finally succeeded in awakening him, telling him to undress and get into bed. The boy recalls this and also that the nurse helped him to remove his clothing.

Dr. Friedrich states that his breathing was normal, but the pulse was very slow; the body was limp, with diminution of the reflexes. There were no changes in the pupils. The boy appeared dazed and his speech was slow and hesitating. The next day he was taken home. The stupor continued without any additional symptoms, except the advent of a temperature of 103.5° F. The abscess had been opened several days before this time and was discharging freely, but giving no pain. He remained in a stupor for a period of four or five days, during which time it was almost impossible to feed him; attempts to swallow were accompanied by cloking, and it was necessary to feed him liquids with a spoon. From the hesitating speech he passed into a condition of complete aphasia, at the end of four days being unable to speak a word. The neck was stiff and the head slightly retracted; pulse very slow, rarely going above 60. There were no signs of ocular or other paralyses. The pupils were equal, of normal size, but reacted very slowly to various stimuli. The nose, larynx, and retinæ were carefully examined by Drs. Friedrich and Lenker and nothing abnormal discovered. No signs of thoracic or abdominal disease could be demonstrated.

His temperature continued irregularly elevated for a period of two weeks. His aphasia remained complete during this time, but he seemed able to understand everything that was said to him; could read print and writing, but he was not asked to attempt writing. There was no numbness, or paræsthesia, or loss of sensation. Before his aphasia became marked he complained bitterly of headache, and later, for a period of two weeks, by gestures continued to attempt to convey to his attendants the idea that the ache continued. If he attempted to get up on his feet he would fall, and he also fell out of bed and was unable to get up when down. After he was up and about his gait was markedly ataxic; he staggered like one intoxicated.

He cried a great deal, especially at the end of the second week, and seemed to be very much excited because he could not make his attendants understand what he wanted. Discovering that he cried because of hunger, his attendants began to feed him, when he developed almost a mania for food; would eat until they were afraid to feed him so much, and then shriek with rage and disap-

pointment because he was not given more.

He was aphasic for a period of five weeks, and when speech returned by slow degrees it was distinctly scanning, slow, and thick. His parents relate that he was very much irritated by the presence of other children in the room and would usually order them out, speaking in a manner that was illustrated by the mother as follows: "You-u g-get r-i-i-ght o-u-ut—of-dis- ro-o-o-m—he-e-r-r"—this being the first formula which he seemed able to enunciate. The parents' and physician's account of this peculiar enunciation fits the apt description of Westphal, who said his patient's words came out as though each syllable was "squeezed out." His speech seemed to return rather rapidly; in fact, he soon insisted upon talking most of the time, but it was very hard to understand him, because of his enunciation being so thick, slow, and scanning.

I examined him in the following November: He is a large, well-developed boy, with hydrocephalic type of head. His eyes are prominent, pupils wide, vision normal; no nystagmus, ocular palsies, or pupillary disturbance; palpebral apertures are wide, showing the sclera above the cornea. His gait is peculiar. He walks like a boy who has on a pair of shoes that are too small for him. His station is not good. His parents state that if he receives a slight push he is unable to recover himself and falls. Knee-jerks are quick, no ankle clonus, no Babinski's sign. Left wrist-jerk and elbow-jerks are more marked than the right. His left hand is the seat of a peculiar movement resembling very closely an athetosis; this is particularly marked while walking. Indeed, his gait is worthy of attention and study. The legs are brought forward awkwardly and stiffly; the toes of both feet turn in, which his parents assure me was not the case previous to his illness. The toe of the left shoe is worn more than the right, and it is believed, when not on exhibition, that he drags this foot a little. The right hand hangs normally at his side, while the left is held partially behind him, the palm directed backward and on a line with the middle of the thigh, and at every step is the seat of a distinct athetoid movement involving the wrist and fingers. His parents inform me that this peculiar movement of the hand is often present while sitting still. All characteristics of chorea are absent, and I believe the movement to be an uncontrollable or athetoid movement consequent upon pathological alterations of the He occasionally complains of headache.

There are now but few pits to be seen upon the face or body, and in a few months little will remain to show that he has suffered from smallpox. The only evidence of his aphasia at present is a certain thickness of speech and a tendency to stumble over syllables; in fact, he stumbles over the syllables in "United Irish Constabulary" as badly as a well-developed case of paresis. There appears to be, however, a slow and continuous improvement. His parents say that he seems to be as bright in school as before, but that his disposition has changed; that he is cranky and irritable. His father states that when children tease him about his tripping speech he weeps, "instead of punching them," as he formerly did when plagued.

There are some rather novel features in this case; some, indeed, suggesting hysteria; and were it not for the slow pulse, high temperature, and bulbar symptoms, one would be justified in suspecting a neurosis. The headache, slow pulse, and stupor point to an intracerebral pressure, probably due to a simple effusion. Assuming an intracercbral pressure, we have an explanation of the bulbar symp-

toms.

The aphasia, which was complete, and has left its mark in a halting speech, and an athetosis, point to an undoubted lesion of cerebral tissue, possibly hemorrhagic, or to areas of localized softening. The spinal symptoms of the case are as clearly marked as in Westphal's

cases, and the clinical ensemble is certainly of that type.

Case II.—A healthy young woman was taken sick with smallpox the last of May, 1902, and was removed to the Detention Hospital. While there she was under the care of Drs. A. B. Spurney and M. Friedrich, to whose courtesy I am indebted for most of the data of the case. She had a good family history and had been quite healthy herself, with the exception of frequent attacks of night terrors, which still continue.

After the usual prodromal symptoms the eruption appeared at about the fifth day, and, although discrete, was widely disseminated and the pocks large and close together. The secondary fever was not high, but the third day following the eruption she became very delirious. The delirium was not entirely characteristic of the ordinary febrile delirium, since it largely partook of the type of religious mania. Shortly after this delirium manifested itself she lost her speech, swallowing became difficult, and she lay helpless in bed; all four extremities were limp and perfectly useless. The urine and feces passed uncontrolled into the bed. Dr. Spurney states that the deep reflexes were absent at this time. Quite a number of abscesses developed, some of which persisted long into her convalescence. Her speech was almost entirely absent for a period of over three weeks, when it began to slowly return and had the same characteristics of the page of

istics of the preceding case.

It was found when she was able to get out of bed that she was markedly ataxic, so much so that she reeled and staggered like a drunken person, and continued to do so for a period of about three months. The speech gradually returned, but her mental degradation was marked and interesting. She appeared and acted like an imbecile. She did not know enough to go to bed, but when sent to her room would lie down on the floor. She did not even know enough to dress herself, and had to be watched closely to prevent her undressing in public. She remained practically in this condition for two months, when a slight improvement began and continued progressively until one day, while in the chapel at prayers, she seemed to rather suddenly acquire her orientation, and from then on began to gain so rapidly that one month later she was able to go out to the Smallpox Hospital in Newburg and aid in the care of patients. Her improvement has been steady since then, and at the present time she has practically recovered all her faculties.

Examination. A recent examination reveals practically nothing, except, perhaps, a slight increase of the knee-jerks, a little slowness and tendency to syllabication of words. Her gait is not as good as before; a slight ataxic condition still obtains. The special senses are

normal.

There seems to be evidence that peripheral neuritis occurs in smallpox with greater frequency than heretofore believed. It was formerly supposed that the few cases observed were of very limited extent and probably related to gross anatomical lesions of contiguous structures. Postvariolous paralysis of the soft palate and structures of the pharynx quite similar to the more frequent diphtheritic affections of those parts have been noted by Curschmann, <sup>74</sup> Leyden, <sup>75</sup> and others.

Combemale<sup>76</sup> has collected ten cases of peripheral neuritis occurring as complications or sequelæ of variola. In all of his cases some speech disorder was remarked, which he evidently believed to be due to palatal paralysis, or paralysis, or ataxia of the organs of phonation. Limited cutaneous anæsthesia and paralysis of single muscles, like the case of paralysis of the deltoid reported by Curschmann,<sup>77</sup> may rarely occur, and are certainly due to peripheral neuritis. Of great interest in this connection is the case of serratus magnus paralysis occurring during a variola observed by James J. Putnam.<sup>78</sup> This was undoubtedly due to a neuritis of the posterior thoracic nerve. Atrophy followed, and there was no recovery.

Vulpian<sup>79</sup> reported a case of paralysis and anæsthesia of the right circumflex, with weakness in the distribution of the same nerve on

the opposite side.

Hitzig<sup>80</sup> has observed a case of double brachial neuralgia, with considerable loss of power; also neuralgia of one arm and shoulder, followed by paralysis of the deltoid alone. All of these cases appeared too early in the disease to be attributed to exhaustion or pressure from decubitus.

Eulenberg<sup>81</sup> has reported a case of partial paralysis of the left facial and both median nerves. The electrical reactions were little

changed and recovery ensued.

Rosenblatt's<sup>82</sup> case of crural monoplegia was undoubtedly of peripheral origin, and, as before stated, it is my belief that Charcot's case of right brachial monoplegia, followed by permanent atrophy of the muscles, was also peripheral neuritis.

I find but one case of multiple neuritis following variola in which a post-mortem examination demonstrated conclusively the correctness of the diagnosis; it is reported by P. Grocco, of Milan. The patient, a young man, six weeks after convalescing from smallpox developed all the symptoms of a multiple neuritis, later pneumonia, and finally died.

Gower<sup>st</sup> mentions a case of polyneuritis following varioloid. The patient died of pneumonia six months later, and the purely neuritic character of the paralysis and atrophy was demonstrated. Since he gives no reference to this case, I believe it to be the one reported by

Grocco.

Joffroy<sup>85</sup> observed a patient who, while convalescing from a grave confluent smallpox, developed violent pains in the left arm and shoulder, which was followed by loss of power and muscular atrophy. Pulmonary tuberculosis supervened; the patient died, and a careful pathological and histological examination revealed a parenchymatous neuritis.

Charcot<sup>86</sup> has recorded a case of atrophy involving the muscles of the right arm consecutive to smallpox. It is possible that this case was a brachial plexus neuritis. Rosenthal,<sup>87</sup> of Vienna, reported a case of true progressive atrophy that appeared six weeks sequential to variola.

Indeed, the variolous poison or the combined infections which are so violently manifested in this disease may produce disturbed functions and actual degeneration of any part of the nervous system.

Functional nerve disturbances are not uncommon sequelæ to smallpox. They are commonly severe and persistent, but usually recover.

Epilepsy following variola has been mentioned by Bicrlingus<sup>88</sup> as early as 1679.

Osler<sup>80</sup> states that rarely epilepsy appears during convalescence

from smallpox.

H. E. Armstrong<sup>90</sup> relates a case of "catalepsy," with waxy mobility and afterward rigidity of the limbs and continuance of consciousness, followed by ecstasy, passing into obscene delirium," finally ter-

minating in unconsciousness and death. The patient was a woman, aged twenty-four years, and in the tenth day of a severe variola, with confluent, crystalline eruption.

Dreyfus-Brisac<sup>91</sup> obscrved an hysterical hemiplegia and hemianæsthesia of the right side disappear at the time of the efflorescence of a

varioloid.

To illustrate the profound effects which smallpox may exert in

the production of neurasthenia, the following case is related:

Case III.—W. S., an unmarried policeman, born in the United States thirty-two years ago, gives a good family history, excepting the pertinent fact that he was born when his parents were at an advanced age. He states that his mother was fifty-four years old and his father sixty-four years old at the time of his birth. The patient suffered a sunstroke at sixteen years, and from that time has been troubled with frequent headaches. He says that while he has been physically strong, yet has had little endurance. He experienced a severe attack of measles at twenty-two years, and at twenty-eight years a violent attack of la grippe, and since has been visited by yearly attacks of the affection at about the same time each year.

Three and one-half years ago he suffered a violent attack of confluent smallpox, and is very badly pitted as a result. He was completely disabled for two months and then returned to light duty, but caught cold and was laid up two months longer, suffering at this time rhoumatic pains and remaining unexplainably weak. He again returned to work, when he suffered further relapse of pain and weakness and general indisposition. From then until two years ago, when the final collapse came, he was rarely able to be on light duty more than a week at a time. Shortly before this collapse he had an attack of severe pain in the left upper chest, which extended down the arm to the tips of the fingers and also across the chest. He suffered from several like attacks, but has had none during the past year. At the time of these attacks he was using a large amount of tobacco, but has not used any during the past year. He dates his complete disability to a time when on his "beat" he was seized with a sudden, unreasoning, and uncontrollable fear-a fear that he was going to die, or something terrible was about to take place. immediately collapsed and was taken home in a carriage, since which time he has been completely disabled. He began losing flesh, became afraid to walk on the street, was unable to ride on the street He waxed irritable, restless, and sleepless; hands became unsteady and trembled, gait became reeling, and heart palpitated violently on exertion, and, in fact, without exertion. His condition became so pitiable and his emaciation so extreme that the medical police official and the medical head of the Health Department in the city in which he was an officer decided that he was permanently and totally disabled. He was retired and placed on the pension roll for life.

EXAMINATION. The patient is a strongly built man, and has so far recovered his former weight that he now registers 175 pounds, instead of 130 pounds, at which weight he was retired. His complexion is florid, hair reddish-brown, and face deeply pitted from smallpox. He is extremely nervous and walks with a peculiar, uncertain, reeling gait, typically and picturesquely neurasthenic. His ears are well placed, eyes on a level, features symmetrical, tongue protruded straight, palate highly arched, with torus; palpebral aperture on the left slightly larger than the right, and the pupil of the right eye is slightly smaller than the left. There is no nystagmus, and, to rough test, no ocular palsies. The pupils react to light and accommodation and consensually. The patient states that, although his vision is good, when he reads a short time he becomes mentally confused. He is slightly short-sighted. Knee-jerks rather weak, but equal; wrist-jerks are normal; a slight jaw-jerk is present. No Romberg. Although he reels in walking, it is not a true ataxia. He appears weak in the knees. The hand grasps are interesting. The right at first registers seventy-five, second attempt sixty, third sixty, fourth fifty-five, fifth and sixth attempts fifty. After an interval of about three minutes the best he can do is fifty-five. The heart muscle is normal; pulse rapid. Thoracic and abdominal viscera normal; urinary examination negative.

Among the functional disturbances we are, perhaps, warranted in placing the isolated cases of diabetes mellitus observed and reported by Freiberg, 92 v. Frerichs, 93 and others.

The occurrence of aphasia, with or without associated paralysis as a complication and as a sequel of smallpox, has been observed.

Arnaud,94 Combemale,95 Saint-Phillippe,96 Jaccoud,97 Curschmann,98 and Myers and Whipham99 have reported such cases. Whether these aphasias are due, when alone, to actual destruction of the brain tissue is doubtful; that they are purely functional exhaustion or intoxication of the cortical cells of the speech centres seems more probable. Breganze's case of aphasia, which occurred at the height of a variola and was complete until he made a single application of electricity, when speech returned, but remained stammering, is both puzzling and unique. He considered the loss of speech due to a cerebral atony from exhaustion of the nutrition of the cells. Notwithstanding the behavior of the speech in returning very like hysteria, we must consider the vocal halt which remained as confirmatory to his idea of its pathology, adding, perhaps, to his hypothesis the suggestion of a toxic exhaustion of the cells of the cortex presiding over emissive speech.

The following personally observed instance of aphasia in an otherwise uncomplicated case of smallpox in a boy, aged seven years, was recently reported at length:101

CASE IV.—E. M., white, was born in the United States, and possesses a good personal and family history. When first seen he

had a temperature of 103.5° F., some coryza, a slight diarrhea, and had vomited. There was no history of exposure to acute infectious disease, and, being informed by the parents that the child had been eating a large amount of sweets on the preceding day, I took the case to be a gastrointestinal disturbance, and treated it accordingly. On the following day the child suddenly went into violent eonvulsions and was more or less convulsed for an hour. The temperature was 103.8° F.; on the next day the temperature remained above 103° F., the child was stuporous, with a coated tongue and flushed face. The respiration was regular. The neck was slightly rigid, but no Kernig's sign was present. There was no rash upon the body, nor could the most eareful examination disclose other signs of disease. He was thought to be in a state of meningismus of gastrointestinal origin. His condition remained unchanged, running a temperature of from 103° F., to 105° F., until the morning of the fourth day, when the characteristic eruption of smallpox appeared upon the face and ealves of the legs. The eruption was discrete, frank, and classical. The temperature immediately fell and the child became conscious, but it was observed that he did not talk. appeared to understand, but could not or would not speak. A very slight secondary fever followed, and the patient made an uninterrupted recovery. For a period of over three months the child never spoke a word. He seemed to have forgotten all the language he had ever learned. His hearing was perfect; the movements of his tongue, palate, and vocal cords were normal. He learned readily enough, and in the eourse of six months was speaking with almost as much fluency as before. It was impossible for obvious reasons to classify his aphasia.

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#### A CASE OF TYPHOID FEVER PRESENTING AN ARTERIAL COMPLICATION—PROBABLY AN ARTERITIS.

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Among the protean complications and sequelæ of typhoid fever, those connected with the circulatory system are of great interest. They were recognized at least as long ago as 1806, when Hildenbrand, in an epidemic of typhoid at Cracow, observed some cases in which gangrene of both extremities resulted. Since that time similar cases have been reported and have been explained as due to venous thromboses or emboli. In 1851 Fabre' suggested that autochthonous arterial thrombosis might account for some of these instances, and subsequently different observers, especially the French, have described the symptoms of thromboses of this variety. Some of the apparent cases, however, occurred in young individuals in whom a complete recovery of the affected part ensued. The following case is one of this nature. In these instances it is suggested that an arteritis only existed, which caused the pulse to be so much obliterated that it was merely not felt. A subsidence of the arteritis restores the patulency of the bloodvessels' lumen and the volume of the pulse is consequently increased, returning generally to its former condition.

The symptoms presented by these cases have been especially well given by Bariè, Potain, and Sallès, but the recent publication of Thayer's article renders a detailed discussion of this subject unnecessary. The symptoms in brief are those of "pain, heat, tenderness, swelling, and even resistance in the course of the artery, with diminution or disappearance of the pulsations and coldness or blueness of the extremity." A complete recovery may be noted in a few weeks, "with the disappearance of all symptoms and return of pulsa-

tion, not only in the peripheral, but in the affected vessels."

Typhoid fever; severe infection; two relapses; an arterial complication in the right upper extremity on the forty-first day of the disease; gradual recovery, with complete return of pulsation in the affected bloodvessels.—P. B., aged nine years, was first seen by me December 2, 1900. He complained at this time of headaches and general weakness. His family history was negative. He had never been a strong child, had suffered much from asthmatic attacks since infancy and was very susceptible to colds. The winter previous he had spent in California without apparent great benefit. Of the ordinary diseases of childhood he had had measles, mumps, and whooping-cough. He thought his present illness began two weeks before I saw him, when he first complained of headaches on coming home from school. Nothing especial, however, was thought of this symptom, and he still kept up and about, although three days ago he said he felt quite weak. One day ago he went to bed, at which time his mother said

<sup>&</sup>lt;sup>1</sup> Cas de gangrène et séparation complète du pied dans le cours d'une fièvre typhoïde, Abeille méd., Paris, 1850, vol. vii. pp. 242, 243 ; and Gaz. méd. de Paris, 1851, 3 S., vol. vi. pp. 539-540.

<sup>&</sup>lt;sup>2</sup> Contribution à l'histoire de l'artérite aigue consécutive à la fièvre typhoïde, Rev. de méd., Paris, 1884, vol. iv., 1, pp. 124-149.

<sup>3</sup> De l'artérite et de la gangrène sèche dans la convalescence de la fièvre typhoïde, Gaz. d. hôp., Paris, 1878, vol. li. pp. 537-539; and De l'artérite transitoire des membres inférieurs dans la convalescence de la fièvre typhoïde. Bull. méd., Paris, 1890, vol. iv. pp. 845, 846.

<sup>4</sup> Note sur un cas d'obstructions artérielle au cours d'un cas de fièvre typhoïde chez l'enfant. Lyon méd., 1893, vol. lxxii. pp. 77-82.

<sup>&</sup>lt;sup>5</sup> On Arteritis and Arterial Thrombosis in Typhoid Fever. 'New York State Journal or Medicine, January, 1903.

he scemed quite feverish. He had had no epistaxis, nausea, vomiting, or diarrhœa.

On examination he was a rather weakly developed and poorly nourished boy. The lips and mucous membranes were of a good color; the tongue was coated with a thick white fur; the temperature was 101.8° F., while the pulse was 100 to the minute, regular in force and rhythm, and of good volume and tension. The lungs were negative on examination. At the apex of the heart a soft systolic murmur was audible, which was not transmitted ontward, but was heard with increasing intensity on passing upward, being loudest at the pulmonie area. The abdomen was not distended, and no rose spots were observed, but on palpation pain was complained of, not localized, but general over the entire abdomen. The spleen was not palpable. A dried blood specimen was obtained for a Widal reaction.

On the following day the report from the Widal was negative. The pain over the abdomen still continued, but was, as before, not localized. Some distention was now first noted, which subsequently proved very obstinate in not yielding to the various means employed for its relief. Because of these abdominal symptoms, leukoeyte counts in the morning and evening were taken. They resulted in readings of 7800 and 7400, respectively. No rose spots were seen until the next day, and the spleen was not palpable until December 12th. The patient was ordered cold baths first, but as he resisted the taking of them so strenuously, cold sponges were next given every three hours if his temperature was over 103.5° F. These also had to be abandoned for a like reason, and cold packs were then tried. If they failed to bring about a satisfactory reduction of the temperature, cold sponges were resorted to and generally proved effectual.

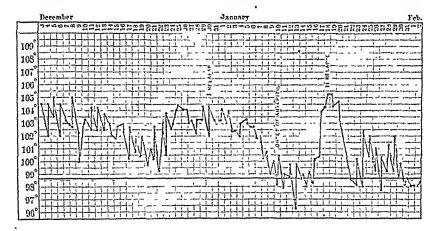
In the matter of feeding great difficulty was encountered, as he objected to taking anything, and the nurses had many a struggle to get him to swallow even a small quantity of liquid nourishment. At one time milk, which was first given him, had to be entirely substituted by broths and egg albumen, as he had a tendency to vomit curdled milk and pass curds in his stools, even with the milk greatly diluted with lime-water. On December 22d, the twenty-second day of his illness, the temperature, which had been gradually falling, reached 99.2° F., and we hoped for a speedy recovery, but a relapse set in, with a temperature of 103.8° F., at 8 P.M., on December 24th, and a subsequent new erop of rose spots. The splech was not apparently palpable, but he did not permit us to make a satisfactory examination. With the relapse he had a marked bronchitis—sibilant, sonorous, and coarse moist rales being heard everywhere over both lungs, especially the right. During this attack warm packs were tried, as he struggled and resisted so against the cold ones, and was frequently quite exhausted after one had been given him. As they seemed beneficial in lowering the temperature, they were continued throughout the course of the disease.

His condition remained satisfactory until January 5th, the fourteenth day of his relapse, when he became quite delirious. At this time his pulse was very small in volume and thready, 124 to the minute. On an examination of his lungs there was slight relative dulness from the angle of the spine of the right scapula, and the breath and voice sounds were here somewhat harsh. Under the stimulation of whiskey and strychnine, the pulse became again full and strong, and later the delirium left him, and the lung symptoms cleared up. The temperature reached normal on the thirty-ninth day of the disease and the eighteenth of his relapse. Two days later, on the evening of the forty-first day, he complained of numbness and tingling of the right index finger. The right radial was of the same force, rhythm, volume, and tension as the left radial, and no swelling or tenderness could be made out along the course of the right radial, brachial, or axillary arteries. There was no stiffness of the right index finger, and movement of the arm did not cause the slightest pain. Uncertain as to what this symptom exactly foreboded, I ordered the arm to be immobilized, and left the patient, thinking the outcome would be a neuritis or an arterial thrombosis. On the following day, January 11th, the right radial pulse was distinctly smaller in volume than the left, but differences between the axillaries and brachials could not be made out. The numbness and tingling had now been transferred mostly to the elbow, and there was also some pain radiating up and down the course of the brachial artery. There was no swelling or sensitiveness to pressure anywhere in the arm. The next day, January 12th, the pulse was wanting in the right radial, brachial, and axillary arteries, which, on account of the patient's emaciation, could be well felt. The skin overlying them was somewhat swollen and looked red and inflamed. Much pain was complained of on palpation, and the axillary and radial arteries had a hard, cord-like feel. The right upper extremity was distinctly colder than the left, and there was some blueness of the finger-nails. The patient's condition otherwise was good. In twenty-four hours the hand became still colder and had a mottled and cyanotic appearance. Dr. William Porter, Jr., of Hartford, who saw the case frequently in consultation with me, and I now became very apprehensive lest gangrene might set in. On January 14th we could get the axillary pulse, but could not feel any pulsation in either the brachial or radial arteries.

For two days his condition remained about stationary, during which period his temperature more nearly approximated the normal, there being but a slight evening rise. But at the end of this time, on January 16th, his temperature rose from 98.2° F. at noon to 100.8° F. at 4 P.M., while his pulse rate increased from 80 to 90 per minute. Coarse mucous rales were heard on this day over the entire right lung, and over the cardiac area a loud, blowing, systolic murmur was plainly audible, being loudest at the aortic area, where it almost completely obliterated the first sound. On examining the abdomen the super-

ficial veins seemed especially prominent. There was much distention and tympanites, which prevented the splcen being palpated for. The arm was extremely cold and the finger-nails intensely evanotic. A fresh crop of rose spots were visible on the following day.

The next few days he grew gradually worse, and soon became intensely delirious. The temperature on January 18th and 19th reached 105.2° F., but thereafter fell slowly until it was 103.5° F., on January 20th at 8 p.m. From this time on until January 22d the temperature was not taken, on account of his extreme delirium and restlessness, which nothing at our command could entirely control. On January 21st the emaciation was so marked, the weakness so intense, the delirium so extreme, and the pulse so small, irregular, and thready that dissolution seemed imminent. The respirations were Cheyne-Stokes in character, the urine was passed involuntarily, and the abdomen was extremely distended. The bowels had not moved for three



days. Under stimulants he rallied somewhat, but the delirium remained. In the next twenty-four hours his condition, though desperate, was a trifle improved, as the pulse was then more regular, and there was no longer Cheyne-Stokes respiration. Food of all kinds was refused, and he was occasionally with difficulty kept in bed. His mouth was dry and parched, sordes covered his lips and tongue, and his breath was foul. There was no change in the arm, save that the cyanosis had disappeared and the difference in temperature, as compared with the left arm, was almost unappreciable. On January 23d, the following day, his delirium ceased, he was able to take some food, and an enema was slightly effectual, much gas being passed. The prognosis became decidedly more favorable.

From this time on his improvement was rapid. The symptoms in the right lung cleared up, and his pulse became good and strong and much reduced in frequency. There was still no pulsation in the right radial and brachial arteries. He was seen on January 26th by Dr. E. G. Janeway, of New York, who expressed a most hopeful

prognosis. The patient's subsequent history was one of rapid progress. On January 31st his temperature became practically normal. Four days later I placed him on a soft diet, and on February 13th, thirty-five days after the onset of the arteritis, I first noted a return of pulsation in the right radial and brachial arteries. The pulse in each was slightly weaker and a trifle slower than in those of the left arm, but in three days I could detect no difference between the two sides. On this day he was placed on solid diet and was allowed to sit up. Shortly thereafter he was permitted to get up and walk about, and I released him from my care.

The urine examinations were negative throughout the course of the disease. I very much regret that I was unable to have another Widal reaction taken.

In considering this case, it seems best to regard the arterial complication as one of the so-called peripheral arteritides, as the symptoms so nearly correspond to those of this nature. The disappearance of the axillary pulsation and its speedy subsequent return may, however, be taken as an indication of the displacement of an axillary thrombus and its later lodgement in the bloodvessels of the brain. This would account for the extreme delirium, but the complete reestablishment of the radial and brachial pulsations is against the view of thrombus formation, and the symptoms of delirium may be well explained by the occurrence of his second relapse.

# THE OCCURRENCE OF CELLS WITH EOSINOPHILE GRANULATION AND THEIR RELATION TO NUTRITION.'

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Many facts are known concerning the activities of the various wandering cells of the blood, yet the significance of few phenomena which they exhibit is clearly understood. Since Cohnheim showed that the polynuclear leukocytes migrate from the bloodvessels, numerous observations have demonstrated how important is the part played by these cells in the inflammatory changes which follow the invasion of bacteria. Nevertheless, we are ignorant of what they accomplish in resisting invasion of the body. Metschnikoff and his pupils believe that the polynuclear leukocytes with neutrophile granu-

<sup>&</sup>lt;sup>1</sup> The present investigation has been conducted with the aid of a grant from the Rockefeller Institute for Medical Research.

lation resist the infective agent by ingesting and destroying it, while other observers, notably Büchner, maintain that the leukocytes furnish something to the fluids which destroys the micro-organism before it is engulfed. The functional significance of the peculiar granules which stud the protoplasm of these polynuclear cells is obscure. Much less is known concerning the activities of a second type of granular leukocyte, the so-called eosinophile cell, and almost nothing is known of its functions. A short survey of its occurrence in various vertebrate species will furnish some indication of its importance.

It is well known that the studies inaugurated by Ehrlich have demonstrated in the leukocytes of the blood distinctive granules which exhibit peculiar affinities for certain dyes or for a whole group of chemically related dyes. Those dyes of which the staining principle is a base distinguish the granules which are characteristic of certain cells. Another kind of granule is stained only by acid dyes. Neutrophile granules, according to Ehrlich, are stained by the neutral mixture of an acid and a basic stain. By the size of the cell, the shape of its nucleus, and the character of the granules scattered in its protoplasm, the various cells of the blood are classified.

By the microscopic study of fresh blood, Wharton Jones¹ was able to distinguish cells with coarse refractive granules, which many subsequent observers believed to be droplets of fat. These coarse granules occupied the attention of Ehrlich² at the outset of his studies upon the staining reactions of protoplasmic granulation. He demonstrated that they are readily stained by all acid dyes, but have such a marked affinity for eosin that when treated with various mixtures of this stain with other acid dyes, they take up it alone. In human blood these so-called eosinophile cells contain a polymorphous nucleus and are actively amæboid, resembling in these characters the more numerous leukocytes, which contain finer neutrophile granules. Eosinophile leukocytes were found by Ehrlich not only in the blood of man and other mammals, but in that of the frog as well, while subsequent studies have demonstrated that they are very widely distributed in the animal kingdom.

ZOOLOGICAL DISTRIBUTION OF CELLS WITH EOSINOPHILE GRANU-LATION. Comparative studies of Hirschfeld' and others have shown that two types of leukocyte with polymorphous nucleus, are present in the blood of all mammalian species. That variety which in almost all mammals constitutes a majority of the white corpuscles and migrating from the bloodvessels plays a very important part in inflammatory processes is provided with relatively fine granules, which exhibit an affinity for acid dyes. Since the common polymorphonuclear leukocytes of human blood contain granules which ex-

<sup>&</sup>lt;sup>1</sup> Philosophical Transactions, London, 1864, p. 63.

<sup>&</sup>lt;sup>2</sup> Verhandlungen der physiologischen Gesellschaft, Berlin, 1878-79, No. 20.

<sup>3</sup> Virchow's Archiv, 1897, vol. exlix. p. 22.

hibit a peculiar reaction to a mixture of certain acid and basic dyes, but have a well-marked affinity for acid stains, they have been designated by Kanthack and Hardy¹ finely granular acidophile or oxyphile leukocytes. The amphophile granules of Ehrlich present in the polynuclear leukocytes of rabbits are stained by both acid and basic dyes. According to Hirschfeld, the more common polynuclear leukocytes of one mammal, the white mouse, exhibit no granulation, but Ehrlich and Lazarus² are inclined to doubt this statement.

Common to all mammalian species examined by Hirschfeld are leukocytes with coarse, acidophile granules. These granules usually exhibit an especial avidity for eosin and are stained by it alone when treated with mixtures containing other acid dyes. Hirschfeld has found that the coarse, acidophile granules of a few animals exhibit a slight modification of this reaction. In the dog and in the cat they take a mixed tint when treated with eosin and aurantia, while in the horse they are stained by eosin and indulin in combination.

Grünberg<sup>3</sup> and Meinertz<sup>4</sup> have studied the white corpuscles of birds, reptiles, amphibia, and fish by the methods introduced by Ehrlich. Small mononuclear cells, with basophile protoplasm free from granules, the lymphocytes of mammalian blood, occur in the various species examined, and forms with polymorphous nucleus are almost constantly found. The latter often contain granules which exhibit an affinity for acid or basic dyes. Cells with acidophile granules are very widely distributed, and in some birds and reptiles constitute a majority of the white corpuscles present in blood. In birds occur two varieties of acidophile granules, both of which show a strong affinity for eosin: (a) round or oval bodies, and (b) peculiar, elongated, spindle-shaped, or crystalloid particles. The latter occur in all birds and in certain reptiles. In the frog the greater number of polynuclear leukocytes are free from granulation, but a minority are studded with round, eosinophile bodies; crystalloid forms are absent. In fish the characters of the white corpuscles and of the granulation they exhibit are very variable. Acidophile granules are frequently found, but often differ in size, shape, and staining reaction from those of higher species. Certain Teleostean fish, for example, Gobio fluviatilis (Mesnil)<sup>5</sup> and Perca fluviatilis (Mesnil and Meinertz), possess no granular leukocytes.

The constant presence among mammals of two types of polynuclear leukocyte, one type being constantly more numerous than the other, suggests the possibility that each form has a peculiar functional significance. In lower vertebrates, namely, in birds, reptiles, amphibia, and fish, this constantly recurring relation is not present.

<sup>1</sup> Journal of Physiology, 1894, vol. xvii. p. 81.

<sup>&</sup>lt;sup>2</sup> Normale und pathologische Histologie des Blutes, Nothnagel's spec. Path. u. Ther., 1900, Bd. viii. Teil, 1.

<sup>Virehow's Archiv, 1901, vol. elxiii. p. 303.
Annales de l'Inst. Pasteur, 1895, vol. ix. p. 301.</sup> 

<sup>4</sup> Ibid., 1902, vol. clviii. p. 353.

Moreover, the color reactions first described by Ehrlich, being doubtless dependent upon certain chemical or physical peculiarities of the specific granulations, afford no proof that structures in widely separated species are anatomically or functionally homologous.

Hence, while the eosinophile cells of mammals, bearing a constant relation in different species, are, doubtless, analogous structures, even though they occasionally present slight variation in their staining reactions, they are not necessarily comparable in function, and other characters to the cells with acidophile or eosinophile granules of lower vertebrates. Such assumption seems to have been made by several writers, who have studied, experimentally, the activities of certain granular leukocytes in frogs and in fish.

Cells with eosinophilic granules form in man a small proportion of the total number of leukocytes; their relative number has been found somewhat variable. Ehrlich has stated that they usually constitute from 2 per cent. to 4 per cent. of the leukocytes, and rarely reach as much as 10 per cent. The figures given by other observers vary within these limits. Zappert, who has very carefully counted the eosinophile leukocytes of healthy individuals, finds the proportion noted by Ehrlich, but, preferring to estimate their absolute number, states that 50 to 250 are usually present in one cubic millimetre of blood, though they may reach 700. In children he found that they are usually more numerous than in adults.

In certain mammals the numerical relation of the eosinophile leukocytes to other forms varies within wider limits. In few species has the proportion been accurately determined. Nevertheless, in two widely separated mammals, namely, in the rabbit and in the dog, accurate counts have been made in the course of repeated experimental studies. Kanthack and Hardy found 1 per cent, to 2 per cent. of eosinophile (oxyphile) cells in the blood of the rabbit; Tallqvist and Willebrand, 30.5 per cent. to 2.8 per cent.; Brinkerhoff and Tyzzer, 40.5 per cent. to 1 per cent. The proportion of eosinophile cells in the dog's blood shows greater variation, and the normal average is higher. In fifteen animals, counts made by Tallqvist and Willebrand varied between 0.2 per cent. and 8.1 per cent., the average being 5.3 per cent. In ten animals Dawson<sup>5</sup> found a minimum count of 2.6 per cent. and a maximum of 21.6 per cent. The individual counts which Dr. Dawson has kindly placed at my disposal are as follows: 6.6 per cent., 12.2 per cent., 2.6 per cent., 21.6 per cent., 4.6 per cent., 5 per cent., 10.8 per cent., 9.4 per cent., 2.6 per cent.

In several instances the count is so much above that obtained from the other animals and from those studied by Tallqvist and Wille-

¹ Charité-Annalen, 1888, vol. xiii.
² Zeit. f. klln. Med., 1893, vol. xxiii. p. 227.

Skandinavisches Arch. f. Phys., 1900, vol. x. p. 37.

<sup>&</sup>lt;sup>4</sup> Journal of Medical Research, 1902, vol. vii. p. 173.

<sup>&</sup>lt;sup>5</sup> American Journal of Physiology, 1900, vol. iv.

brand that the presence of some pathological process to explain the apparent eosinophilia has been suspected. The frequency with which dogs are infected with animal parasites is well known, and uncinaria caninis is found with great frequency in the small intestine. With these facts in view, I have studied the blood of ten apparently healthy dogs, and have subsequently examined the intestines and other organs.

TABLE I.

No.	Leukocytes in 1 c.mm.	Eosinophiles in 1 c.mm.	Parasites in small intestine.
1	15,100	1208 = 8.0 %	U. caninis (3), tænia cucumerina (10 grm.).
2	22,350	939 = 4.2 "	U. caninis (25 to 50) and several tapeworms.
3	16,600	880 = 5.3 "	U. caninis (3), ascaris marginata (1), and small tapeworms in large numbers.
4	15,800	632 = 4.0 "	U. caninis (12) and several tapeworms.
5	10,700	567 = 5.3 "	T. cucumerina (large amount), A. marginata (3).
6	15,400	493 = 3.2 "	T. serrata (large amount).
7	14,200	454 = 3.2 "	Several small tapeworms.
8	16,400	328 = 20 "	A. marginata (10) and two tapeworms.
9	19,700	197 = 1.0 "	U. caninis (3).
10	5,800	24 = 0.5 "	

The figures are inconclusive, since in no instance does the proportion of eosinophile cells equal that noted by Dawson. Nevertheless, they afford a basis for further comparison and suggest, at least, that the absolute number of eosinophile cells bears some relation to the number of animal parasites within the intestinal tract, especially when it is noted that the smallest number of eosinophile cells was found in two animals, one of which contained three parasites (No. 9), while the other (No. 10) was free from infection.

METHODS. Few observations have been made upon the occurrence of eosinophile leukocytosis in lower animals, and while in a few instances experimental eosinophilia has been produced, the progress of the phenomenon has seldom been recorded by repeated differential counts, which are very laborious and time-consuming. In order to avoid, in some part, this difficulty, and at the same time to obtain a great number of observations upon the behavior of the eosinophile cells under a considerable variety of conditions, I have adopted the simple method of counting the leukocytes in fresh blood. Hardening and staining being obviated, the results are of necessity obtained without delay.

A drop of blood is allowed to spread between cover-slip and slide and is immediately examined with the oil immersion lens  $(\frac{1}{12} \text{ obj.})$ . Certain precautions are essential in order to make the white corpuscles so conspicuous that none are missed in counting. Of first importance is the use of artificial illumination, preferably that from the so-called Welsbach burner, since by this means the refraction of the corpuscles is increased and the characters of their granulation and of their nuclei become evident. A diaphragm with a rectangular opening is so inserted into the eye-piece of the microscope that the

upper and lower segments of the field are obliterated and the count, performed with the aid of a mechanical stage, is confined to a somewhat narrow equatorial zone. It is obviously necessary to use only those specimens in which the blood is spread into a moderately thin layer, and to make the count immediately after the blood is drawn.

If these precautions are taken, on the one hand, few, if any leukocytes, are omitted from the count, while, on the other hand, the individual forms, notably the highly refractive eosinophile cells, are recognized with ease and their relative number noted. In most instances this percentage count was limited to the eosinophile cells, since they alone occupied attention and numerous observations, consuming much time, were necessary. As a routine the number of eosinophile cells in 300 or 400 leukocytes was determined. The character of the charts, which will be subsequently described, sufficiently vindicate the accuracy of the method and show that, even though it may not be absolutely exact, it gives an adequate presentation of the changes which the eosinophile lenkocytes undergo. For comparison, I have counted by both methods specimens from five guinea-pigs and from five healthy men.

				Fr	esh	specimen.	Hardened specimen.1
From	n guinea-pig					15.3	14.0
"	"					8.7	10.2
"	"					6.7	5.0
"	"					1.7	3.0
"	44					1.3	0.5
**	healthy man					10.0	8.4
**	ü					3.3	3.2
"	41	•				2.7	2,7
"	"					2.0	2,6
"	"					1.3	8,7
							•

The proportion of eosinophile cells noted in the fresh specimen is not with constancy greater or less than that obtained from the hardened film. Doubtless the ordinary method of counting hardened and stained specimens is accurate only within certain limits. Thus, Boycott and Haldane, making for the sake of comparison successive differential counts of 1000 cells in the same film, found in two cases the following figures for the neutrophiles in four successive thousands of white corpuscles:

59.2	55.5	55.2	53.6 %
-	00.0	****	
35.8	32.7	38.7	34.8 "

For the purpose of certain experiments not included in the present paper, the guinea-pig was found more available than either the rabbit or the dog. Blood can be repeatedly obtained from the peripheral circulation by puncturing the skin of the ear or by nicking with sharp scissors the edge of the ear after clipping the hair.

<sup>&</sup>lt;sup>1</sup> For assistance in counting these specimens I am indebted to Dr. Ernest Cullen.

<sup>&</sup>lt;sup>2</sup> Journal of Hygiene 1903, vol. iii. p. 95.

It was soon found that the number of eosinophile leukocytes was so variable that a preliminary study of the conditions which influence them was necessary. Even though the facts concerned refer to a single species, they are, I believe, of sufficient general interest to justify a detailed study.

Eosinophile Cells of the Blood. The white corpuscles of the guinea-pig, which have been the subject of special study by Kurloff, present several noteworthy peculiarities. In briefly describing the various types, I will mention characteristics observable in the freshly

drawn blood. The following forms occur:

1. Polynuclear leukocytes with fine acidophile granulation constitute, Kurloff states, 40 per cent. to 50 per cent. of the total number of white cells. According to Ehrlich and Kurloff, the granulation is of the pseudoeosinophile or amphophile type, but Hirschfeld denies this statement and claims that the granules stain only with acid dyes, and, preferably, with indulin.

2. Eosinophile cells are readily recognized in fresh blood by their coarse, round, or oval, very refractive granules of somewhat greenish tint; they are very actively amœboid. In stained specimens the nucleus is often found to be horseshoe-shaped or trilobed, while all

transitions between the two occur.

3. Basophile cells can be identified in the fresh specimen. They are filled with coarse, oval granules, which are easily distinguished from those of the eosinophile cell, being of greater size and only slightly refractive. These cells are actively amæboid at tempera-

tures approximating that of the body.

4. Lymphocytes resembling those of human blood constitute, according to Kurloff, 30 per cent. to 35 per cent. of the total number of white corpuscles. Large and small mononuclear cells occur. I have frequently observed amœboid movement, but it is much less active than that of the forms previously mentioned. A short protrusion of the protoplasm occurs at one point. The projection becomes larger and knob-like, constricted where it joins the remainder of the cell. This constriction persists and passes like a wave from one side of the cell to the other as the projecting protoplasm increases at the expense of that which remains.

5. Vacuolated cells peculiar to the guinea-pig have been described by Kurloff and represent a considerable proportion of the mononuclear leukocytes. Within the protoplasm are one, or, occasionally, two globules, which, in fresh specimens, have a homogeneous, greenish color, and are more refractive than the cell protoplasm; the globule is frequently larger than the nucleus of the cell. Such

vacuolated cells are inactively amedoid.

In order to obtain a basis for comparison, the occurrence of eosinophile leukocytes in the blood of normal guinea-pigs has been studied

and their distribution in the internal organs has been observed. Kurloff states that eosinophile cells constitute only 1 per cent. of the white corpuscles of the blood; Kanthack and Hardy give the proportion as 2 per cent. to 3 per cent. Finding these figures much exceeded in many apparently healthy animals, I have been inclined to suspect the presence of some latent pathological process. Postmortem examination has failed to confirm this suspicion, though the possibility cannot be excluded with certainty. The intestine of the guinea-pig is subject to infection with several protozoan parasites, which apparently produce no noteworthy alteration of health. the small intestine one not infrequently encounters the flagellate parasite, megastoma entericum, while in the cocum infusoria are almost constantly present, often in considerable number. No relation was established between the presence of these protozoan forms and the occurrence in the blood of eosinophile leukocytes in unusually large numbers. The frequency with which eosinophile cells are found in the lungs, and notably in the wall of the bronchi, has directed especial attention to these organs. The relation of the eosinophile cells in the blood to those of the bronchi will be considered later.

Animals with high eosinophile count have been often found to be especially large, healthy specimens, and, indeed, a relation between the number of eosinophile cells and the weight of the animal is readily established. In the following table, in which the animals are ranged according to their weight, is recorded the preliminary count made upon many healthy animals previous to performing various experiments:

	TABLE II.										
Wt.	Eo. %	Wt.	Eo. %	Wt.	Eo. %	$\mathbf{W}t.$	Eo. %	Wt.	Eo. %	Wt.	Eò. %
299	0.6	398	0.0	481	1.3	546	16.0	667	2,3	785	19.3
287	0.0	363	0.3	436	0.3	509	0.0	615	1.5	788	15.0
		309	0.0	400	1.5	501	1.0	653	3.3	718	8.7
		385	0.3	454	0.3	556	1,3	622	4.0		
		366	1.7	423	1.3	597	29.0	649	15.3		
		345	1.7	418	0.0	567	5.7	665	9.0		
				491	0.0	586	6.7	622	36.3		
				497	0.0	578	5.7	604	10.3		
				406	0.5	532	9.7	650	7.3		
				415	0.0	588	6.8	625	24.3		
				487	5.7			672	1.5		
								697	15.0		
								641	18.0		
								604	8.3 •		
Mean	, 0.3		0.6		1.1		8.2		11.2		14.3

In the foregoing table certain facts are noteworthy. In animals weighing less than 500 grams the proportion of eosinophile leukocytes rarely exceeds 2 per cent., and agrees approximately with that found by Kurloff and by Kanthack and Hardy; but in animals of greater weight a much higher percentage is almost constant. Even where the animal weighs more than 500 grams the proportion is

occasionally less than 2 per cent., but the mean for animals of this weight is much higher. The averages have been calculated from the figures in the various columns of the table, each of which, from left to right, represents an increase of 100 grams. After a very slight gradual increase in the proportion of eosinophile cells, reaching 1.1 per cent. for animals weighing from 400 to 500 grams, there is a sudden rise to 8.2 per cent. in the next column, followed by a more gradual increase in the columns containing guineapigs of greater weight. The animals, which in almost every case had been obtained from dealers only a short time before examination was made, had doubtless been subjected to varying conditions of nutrition. This fact, as will be subsequently shown, may account for some variation in the percentage of eosinophile leukocytes.

The great variation to which the number of eosinophile leukocytes in the blood of apparently healthy guinea-pigs is subject is further shown by the following table, in which in ten instances their number in one cubic millimetre of blood has been calculated from the total number of leukocytes:

TABLE III.

No.		w	eight.	Leukocytes in 1 c.mm.	Eosinophiles in 1 c.mm.				
1.					454	8,100	24	= 0.3 %	
2.					521	8,700	1479	= 17.0 "	
3.					532	10,600	1028	= 9.7 "	
4.					556	16,600	249	= 1.5 "	
5.					578	24,200	1379	= 5.7 "	
6.					625	8,500	2916	= 34.3 "	
7.	•				650	12,500	913	= 7.3 "	
8.					690	15,700	1649	= 10.5 "	
9.					695	13,900	2127	= 15.3 "	
10.					718	10,800	940	<b>≈</b> 8.7 "	
	Mean					12,960	1270	= 110 "	

The total number of leukocytes varies within such wide limits that the proportion of eosinophile cells allows only a rough estimation of their absolute number. Nevertheless, if the figure which represents the percentage count is multiplied by 115 (the mean number of eosinophile leukocytes in one cubic millimetre of blood divided by the mean percentage count), a figure approximating the absolute number of eosinophile leukocytes is obtained. Hence the facts demonstrated by Table II. are applicable to the absolute as well as to the relative number of these cells.

Eosinophile Cells in the Tissues. The distribution of eosinophile cells in the organs of the guinea-pig still further indicates that they play a very important part in metabolism. Heidenheim¹ has shown with what frequency these cells are found in the mucosa of the dog's intestine, while Teichmüller² has emphasized

<sup>&</sup>lt;sup>1</sup> Pfluger's Areh. f. Phys., 1888, vol. xliii. Suppl. Hft.

<sup>&</sup>lt;sup>2</sup> Deutsehes Arch. f. klin. Med., 1898, vol. lx. p. 576.

their abundance in the lungs. Their distribution in the organs will be briefly described.

Throughout the gastrointestinal tract eosinophile cells occur in great abundance and are most numerous in that part of the mucous membrane which is between and immediately below the tubular glands. They are readily recognized in sections stained with eosin by their large, oval, brilliantly red granules. They do not differ from the eosinophile leukocytes of the blood and are provided with nuclei which are trilobed, bilobed, or horseshoe-shaped.

In the superficial part of the gastric mucosa eosinophile cells are scant, but are very numerous between the ends of the glands and in the narrow zone between the glands and the muscularis mucosæ. In the submucosa immediately below the muscularis mucosæ they are again abundant, but elsewhere in the connective tissue of the

gastric wall are rarely found.

Throughout the mucous membrane of the small intestine eosino-phile cells are found between the bases of the glands of Lieberkühn, in the subglandular tissue which lies between these glands and the muscularis mucosa, but are scant in the villi and in the submucosa. Such cells are especially numerous in the mucosa overlying the Peyer's patches. In the guinea-pig a diverticulum of the superficial epithelium extending downward is situated just above each constituent follicle, and in the lymphoid tissue lying between two such diverticula eosinophile cells are not infrequently so numerous that they give a red color to the tissue examined with the low power of the microscope. In the mucosa of the large intestine, and especially in the execum, cells with eosinophile granules are numerous between the bases of the glands.

In the walls of the trachea, the bronchi, and the subdivisions of the latter eosinophile cells are found in considerable number; in the connective tissue surrounding the bronchi and the bloodvessels similar cells occur, while not infrequently they are present in the

interalveolar walls outside the capillary vessels.

Of considerable interest is the readily demonstrable fact that eosinophile cells penetrate through the epithelium into the lumen of the small bronchi. Scattered in the loose areolar tissue of the mucosa may be found cells with eosinophile granulation, and between the columnar cells of the epithelium similar eosinophile cells are easily recognized, while others have made their way into the lumen of the bronchus. Cells with scant, partially disintegrated protoplasm, containing a somewhat irregular nucleus, are usually more numerous in the same situation. The possibility that some of these nuclei represent the remains of eosinophile cells altered by the bronchial secretions has occasionally suggested itself, but the occurrence of such transformation has not been demonstrable.

Eosinophile cells are at times even more numerous in the fibrous tissue external to the muscle than in the mucosa. Should a small

nodule of lymphoid tissue occur in this situation, eosinophile cells show an especial tendency to accumulate in the part of the nodule which is next the lumen of the bronchus and in the tissue immediately overlying. Throughout the external coat of connective tissue eosinophile cells are numerous. A specimen in which eosinophile cells were particularly numerous has served to explain the origin of these cells, for in the small bloodvessels of the bronchial wall they are very numerous, probably held here by some chemotactic influence. They doubtless emigrate not only from the small veins of the connective tissue, but from the alveolar capillaries in the immediate neighborhood of the bronchus, for in these vessels they are present in much greater numbers than in the interalveolar capillaries more distant from the bronchus.

The passage of eosinophile leukocytes into the bronchi probably exerts an influence upon the number of eosinophile cells in the blood. Examination has not been made in a sufficiently large number of animals to determine the relation of the process to the eosinophilia noted in apparently normal guinea-pigs. In six of nine animals I have found eosinophile cells within the lumina of the bronchi; the weight and proportion of eosinophile cells in the blood were as follows: (1) 650 grams, 7.3 per cent.; (2) 625 grams, 24.3 per cent.; (3) 622 grams, 36.3 per cent.; (4) 604 grams, 8.3 per cent.; (5) 556 grams, 1.5 per cent.; (6) 521 grams, 17 per cent. In the three remaining animals no eosinophile leukocytes were found within the bronchi; their weight and percentage of eosinophile leukocytes were as follows: (7) 643 grams, 5.7 per cent.; (8) 454 grams, 0.3 per cent.; (9) 390 grams, 0.5 per cent.

In large, apparently healthy animals eosinophile cells migrate from the bloodvessels into the bronchi, and there is, as far as I have found, no additional evidence that the bronchi are the seat of a pathological process. The significance of this migration is not

apparent.

Below epithelial surfaces other than those of the intestine and airpassages, eosinophile cells are rarely found. They do not accumulate below the squamous epithelium of the normal skin, nor of the tongue, in the mucosa of the bladder, nor in the walls of the ducts

of the liver, pancreas, or testicles.

Kanthack and Hardy claim that the connective tissue is the especial habitat of the coarsely granular oxyphile cell, yet only in certain localities are they constantly present in considerable number. Cells with eosinophile granulation are infrequently observed in the subcutaneous areolar tissue, in the fascia and septa of muscles, and in the connective tissue of the liver, kidneys, adrenal glands, pancreas, thyroid, and testicles. In the serous membranes, the omentum and the mesentery, on the contrary, eosinophile cells are fairly numerous and are distributed in greatest number along the course of the small bloodvessels. Within the serous cavities, as Kanthack and Hardy

have shown, these cells are constantly present and constitute from 30 per cent. to 50 per cent. of the total number of cells in the peritoneal fluid of the normal guinea-pig.

Little attention has been paid to the intimate relation which exists between the lymphatic apparatus and the cosinophile cells. Their abundance in the lymphoid tissue of the gastrointestinal mucosa has already been noted and attention has been directed to their accumulation in the Peyer's patches of the small intestine and in the lymphoid follicles of the bronchi. Their presence in the serous cavities is noteworthy. They are, moreover, constantly present in the lymphatic glands, not only in those at the base of the mesentery, but in the peripheral glands, such as those in the inguinal region as well. Eosinophile cells are not found within the follicles which occupy the cortex of the gland, but are fairly abundant at the periphery of the follicles, near and at times within the peripheral sinus. Within the sinuses of the medullar cords they are more numerous and are not infrequently ranged along the margins of the sinuses.

In the connective tissue in the immediate periphery of the lymphatic glands eosinophile cells are often found in abundance, and their number diminishes as the distance from the gland increases. In one specimen, by a fortunate accident, I obtained evidence that these cells are derived not from the gland, but directly from the blood. Cells with eosinophile granulation were here numerous, both in the tissue and in the small veins, and had been actually fixed in process of migration from the latter. In several instances elongated eosinophile leukocytes had partially penetrated the endothelium of

the vessel, part still remaining within the lumen.

In the bone-marrow cells, with coarse eosinophile granulation, are more numerous than in any other organ of the healthy animal. Here alone are found the large mononuclear eosinophile cells described by H. F. Müller and Rieder. They are analogous to the myelocytes of Ehrlich, which are essentially cells of the bone-marrow and only in leukæmia find their way into the general circulation. The myelocyte with eosinophile granulation is considerably larger than the eosinophile leukocyte, and is provided with a large round or oval, often irregularly indented nucleus. In sections of marrow hardened in Zenker's fluid the nuclear membrane stains deeply with hæmatoxylin, giving a vesicular appearance to the nucleus, but chromatic substance is not abundant, so that the nucleus, particularly in dried preparations, stains palely. Müller and Rieder have shown that these cells are capable of little if any amœboid movement.

In addition to invelocytes with eosinophile granulation, smaller eosinophile cells with polymorphous nuclei are present in the bone-marrow. Many of these are identical with the eosinophile

<sup>1</sup> Deutsches Arch. f. klin. Med., 1891, vol. xlviii. p. 47.

leukocytes of the blood and are capable of amæboid movement. Cells of the same size may contain a rounded nucleus, which is usually kidney-shaped as the result of an indentation at one point. Other small eosinophile cells have a nucleus which has the form of a bent rod; constrictions at intervals so divide the rod that it is transformed into the lobed nucleus which is found in the eosinophile leukocytes of the circulating blood.

Mitotic division of eosinophile cells in mammals was first described by H. F. Müller, though similar observations had been made by Flemming<sup>2</sup> and Dekhuysen<sup>3</sup> in amphibia and birds. Such division in the guinea-pig takes place only in the bone-marrow and occurs in cells which are usually so large that they are recognized as

myclocytes.

Corresponding to the varying number of eosinophile cells in the circulating blood of guinea-pigs, the bone-marrow exhibits variations which help to explain the origin of these cells. In animals of which the blood during life contains approximately 1 per cent. of eosinophile leukocytes fat is very abundant and the cells of the marrow occupy the interstices between the fat-cells. Eosinophile cells of the characters already described occur in moderate numbers scattered among the other cellular elements. In animals with a larger proportion of eosinophile cells in the blood, similar cells are more numerous in the marrow, but in guinea-pigs in which the cosinophile cells of the blood reach the proportion of from 15 per cent. to 30 per cent. the bone-marrow presents a characteristic appearance. The fat is in great part or wholly replaced by myeloid tissue, which is largely composed of cells with eosinophile granules. Myelocytes are particularly numerous, but smaller cells with polymorphous nucleus are not wanting. Eosinophile cells in process of mitotic division are readily recognized by the hyperchromatic condition of the nucleus, and never in large numbers, are much more numerous than usual; the so-called diaster stage of mitosis is not infrequent.

In the pulp of the spleen eosinophile cells are found in considerable number, and are more abundant the greater the number in the circulating blood. They are absent within the Malpighian corpuscles, but are particularly abundant in the pulp at their periphery. Eosinophile myelocytes do not occur and mitotic figures are not demonstrable.

Relation of the Eosinophile Cells to Nutrition. In apparently healthy guinea-pigs weighing more than 500 grams, eosinophile leukocytes, as it has been shown, not infrequently form from 15 per cent. to 30 per cent. of the total number of leukocytes, and in the greater number of instances constitute 8 per cent. to 14 per cent. In this animal, more readily than in man, where the eosinophile cells rarely exceed 4 per cent., it is possible to deter-

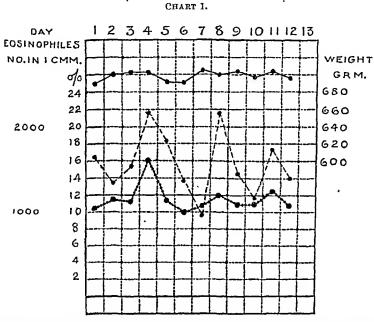
Arch f. exper. Path. u. Phar., 1892, vol. xxix. p. 221.

<sup>&</sup>lt;sup>2</sup> A.ch. f. mik. Anat., 1891, vol. xxxvii. p. 249.

<sup>&</sup>lt;sup>3</sup> Anat. Anz., vol. vi. p. 220.

mine the conditions with which these cells are diminished, as well as those with which they are increased.

It was considered desirable to make a preliminary study of the changes to which the eosinophile leukocytes may be subject under ordinary conditions. For this purpose the blood of guinea-pigs supplied with abundant food and water were examined repeatedly for a considerable period of time, and variations in the number of eosinophile cells were noted. The animals were allowed to feed at will and no allowance was made for a possible leukocytosis of digestion. The records which follow indicate that such leukocytosis is not an important disturbing factor. The weight of the animal serves as the best indication of its condition and has been recorded in conjunction with the count of eosinophiles.

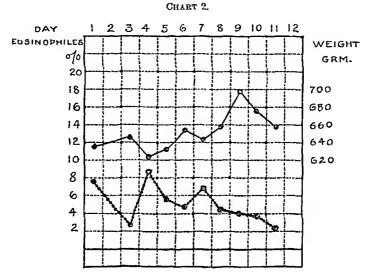


In this and in the charts to follow the percentage of eosinophile cells is represented by a dotted line, their number in one cubic millimetre of blood by a broken line. The weight of the animal is represented by a black line.

In Chart 1 are recorded the weight of the animal, the proportion of eosinophile cells in the blood, and their absolute number in one cubic millimetre of blood, calculated from the total number of leukocytes, which have been estimated daily by means of a Thoma-Zeiss apparatus. During twelve days the weight has varied little, ranging from 690 to 705 grams. The proportion of eosinophile cells exhibits slight variations, which correspond fairly well to much more marked alterations of their absolute number. At intervals of several days there is a recurring increase in the number of these cells, as though

many were rapidly thrown into the circulation. The sudden elevation of the curve is followed by a somewhat more gradual fall.

In Chart 2 only the weight and proportion of eosinophile cells are recorded.



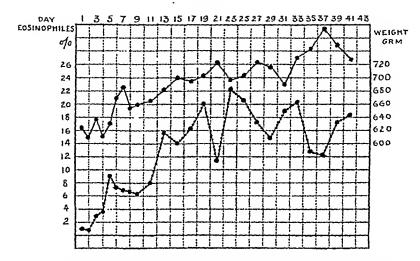
The weight of the animal varies within wider limits than that recorded in Chart 1, and, as in the previous instance, the proportion of eosinophile cells alternately increases and decreases. A comparison of the two curves suggests that the number of eosinophile cells bears a relation to changes in the weight of the animals, for repeatedly an increase in weight is accompanied by a fall in the proportion of eosinophiles, while a decrease of weight is accompanied by an increase in the number of these cells, so that the two curves tend to vary in opposite directions. This phenomenon is not constant, for on the tenth and eleventh days, though the weight has fallen, the eosinophiles do not rise. Doubtless, conditions other than those which affect nutrition exert an influence on the proportion of eosinophile cells, and in Chart 1, though the number of eosinophile leukocytes varied considerably, the weight changed little.

A relation between variations in weight and proportion of eosinophile cells is even better indicated in the following curve, where the eosinophile leukocytes rose gradually during a period of nearly three weeks. Alterations of the number of eosinophile cells, with much constancy, take an opposite direction from those of weight, and at times these contrary variations extend over a period greater than a week.

There was reason to suspect that the animal of which the number of eosinophile cells is recorded in Chart 3 had received, just before these observations were begun, an insufficient amount of food. The possibility has suggested itself that the food supply may exert an influence upon the eosinophile leukocytes of the blood.

By the use of Ehrlich's triple stain somewhat modified Heidenhain demonstrated the existence of cells with deep-red granules, undoubtedly eosinophile cells, in the villi, and still more abundantly in the subglandular layer of the dog's intestinal mucosa, and studied





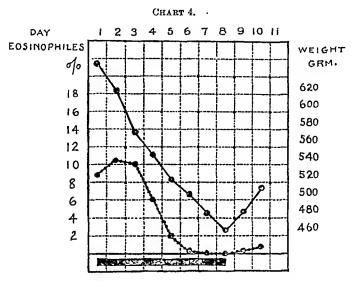
these cells under varying conditions of nutrition. If animals were starved during from four to seven days and then killed, eosinophiles disappeared from the villi and their number in the subglandular layer was diminished. Considerable variation was noted in individual cases, and in one instance eosinophile cells were numerous even after some days without food. Abundant feeding produced the opposite condition; if a dog receiving an ordinary diet was given a large meal of meat and was killed fourteen to sixteen hours later eosinophile cells were found in very large numbers, both in the villi and in the subglandular layer. Sugar in large amount had the same effect as proteid diet. Continued overfeeding diminished rather than increased the number of cells with eosinophile granulation.

Teichmüller repeated with guinea-pigs some of the experiments of Heidenhain. He found that starvation causes the number of eosinophile cells in the intestinal mucosa to diminish, but thought that the number in the spleen was increased. If, however, the animal was killed by starvation, eosinophiles were diminished in the intestine, spleen, and bone-marrow. Hence, he reached the conclusion that starvation causes a temporary increase of eosinophile cells, followed by diminution of their number.

As far as I have been able to determine, observations upon the eosinophile cells of the blood during starvation have been made only by Tanszk, who observed the fasting juggler Succi. An increase in the proportion of eosinophile leukocytes was noted.

<sup>1</sup> Wiener klin. Rundschau, 1896, No. 18. Quoted by Teichmuller.

Following the suggestion offered by Chart 3, I have studied the effect which withdrawal of food exerts upon the eosinophile leukocytes of the circulating blood. The consequent changes are well shown in the following chart.



In this and in the charts to follow the period during which the animal received no food is indicated by a broad black line at the bottom of the chart.

Though the weight diminished continuously from the beginning of the experiment, there was a primary increase in the proportion of eosinophile leukocytes, but after the third day they also decreased in number, and on the seventh and eighth days none were found in the specimens of blood which were examined. Estimation of the total number of leukocytes in conjunction with the proportion of eosinophile cells in two animals from which food was withheld has shown that diminution of the absolute number of eosinophile cells is accurately represented by the preceding chart, which records only their relative number.

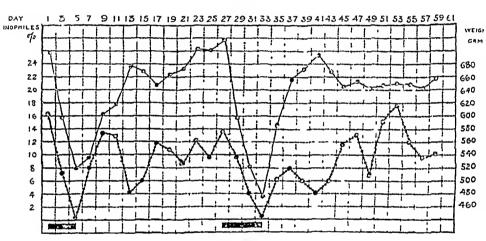
•										
				Gun	NEA-PIG A.					
]	Day.			Weight, grm.	Leukocytes in 1 c.mm.	Eosinophiles in 1 c.mm.				
1st .				. 712	11,900	1428	=	12.0 %		
2d .				. 677	8,600	1075	==	12.5 "		
3d .	•			. 645	14,200	2087	=	147"		
4th.	•	•	•	. 619	10,600	1325	===	12.5 "		
	•	•	•	E04	15,500	852	=	5.5 "		
5th.	•	•	•	. 394	10,000					
				Gui	NEA-PIG B.					
1st .				. 650	7,900	869	=	11.0 "		
2d .				. 615	12,900	1741	=	13.5		
3d .	•			. 579	12,000	840	_	7.0 ''		
4th.	•	•	•	EED	17,500	787	==	4.5 "		
	•	•	•	506	10.900	414	==	3.8 "		
5th.	•		•	. 020	10.300	71.		0.0		

In both experiments an increase in the relative and in the absolute number of cosmophile leukocytes preceded the fall, which

began on the fourth day of starvation.

If food is withheld during several days, the animal may loose in weight 100 or more grams, and, gradually recovering, regain its former size only after several weeks. With the administration of food there is a sudden increase both of weight and of eosinophile leukocytes, but the increase of neither is uninterrupted. In the experiments recorded by the accompanying chart, withdrawal of food on two occasions, namely, from the first to the fifth days of observation, and again from the twenty-seventh to the thirty-third day, has been followed by a fall of eosinophile leukocytes to less than 1 per cent.





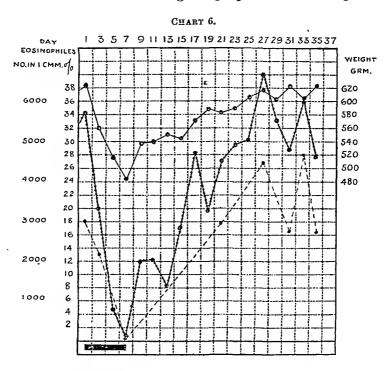
During the period which follows the administration of food the chart exhibits the phenomenon which has been noted in the normal animal. Increase in the proportion of eosinophile leukocytes is not continuous, and after two or three days their number falls, even though the weight, which is yet far from normal, continues to rise. Soon the increase of weight is interrupted, and with a fall in the curve of weight there is an increase in the proportion of eosinophile cells. This phenomenon is conspicuous during the first ten days or two weeks after starvation, but may be subsequently absent.

In the experiment recorded in Chart 6, an animal was employed of which the blood contained eosinophiles in the unusual proportion of 34 per cent.; the total number of leukocytes was, however, some-

what less than usual.

In this experiment the eosinophile leukocytes did not fall to 1 per cent. until the seventh day after food had been withdrawn; the weight diminished during this time 140 grams. The subsequent rise and fall of the curves representing weight and eosinophile cells

show the remarkable relation previously observed, though the falls in weight on the nineteenth and again on the twenty-fifth day, with which in each case corresponds a sudden rise in the proportion of eosinophile cells, are so slight that they may be regarded as interruptions of the gradual return to normal. The total number of leukocytes was estimated at intervals, in order to determine the absolute number of eosinophile cells in one cubic millimetre of blood, but no important difference between the proportion and the absolute number of eosinophile leukocytes was observed. Particularly noteworthy is the fact that variations affecting the proportion of eosinophiles, and



occurring between the thirty-first and thirty-ninth days, when the animal's weight had become normal, correspond to inverse variations of weight, and represent the absolute as well as the relative number of eosinophile cells.

In three animals I have studied in sections from tissues hardened in Zenker's fluid the effect of starvation upon the distribution of the eosinophile cells. The weight, the percentage of eosinophile leukocytes at the beginning of the experiment, and the date of death were as follows:

No.	1.	Weight, 385 grm.			Percentag	Killed on the 5th day.						
**	2.	11	712	"	"	46	• •	12.0.	"	**	6th	"
"	3.	**	650	"	**	**	**	11.0.	**	"	8th	"

Except in the animal killed on the eighth day of starvation, there was no noteworthy diminution in the number of cells with eosinophile

granulation in the wall of the small intestine, and especially in the Peyer's patches. On the eighth day, however, their number had appreciably diminished. In the mesenteric lymph glands and in the connective tissue of the mesentery and omentum, on the contrary, few such cells were found in any of the animals examined. The same statement can be made concerning the lungs where eosinophile cells are usually so abundant. The number in the spleen was much diminished, and, as usual, was in close relation with the number present in the blood.

In order to determine what changes have taken place in the bone-marrow, it is necessary to recall the fact that the number of eosino-phile cells here present is variable and has a relation to the proportion of eosinophile lcukocytes in the blood. In no case was a note-worthy diminution observed in this organ. In the animal killed on the fifth day, in which the eosinophile leukocytes at the beginning of the experiment numbered only 3 per cent., eosinophile cells were fairly abundant in the marrow and were, in great part, of small size, with polymorphous nuclei; myelocytes were not numerous. In the animals killed on the sixth and eighth days eosinophile cells were still present in great abundance, and smaller forms, resembling those usually found in the circulating blood, were far more numerous than myelocytes with eosinophile granulation. Particularly noteworthy is the fact that the eosinophile cells of the bone-marrow do not show the marked diminution which occurs in other organs.

ORIGIN OF THE EOSINOPHILE CELLS. Ehrlich has maintained that a sharp distinction can be drawn between the lymphocytes and the granular leukocytes; the former have their origin in the lymphatic glands and in other tissues which form part of the lymphatic system, while the latter are derived wholly from the bone-marrow. The great number of eosinophile cells present in the bone-marrow furnishes evidence, Ehrlich has maintained, that they here undergo multiplication. Other observers (Müller and Rieder) have suggested that their presence may be explained by supposing that the bone-marrow is a storehouse for eosinophile leukocytes.

Max Schultze, who, almost forty years ago, classified the leukocytes observable in fresh blood studied upon a warm stage, reached the conclusion that the amœboid cells containing coarse granules are derived by gradual transition from the amœboid leukocytes with fine granules and many subsequent writers, including Ouskow, Zappert, Müller and Rieder, Gulland, and Van der Stricht, finding in human blood what they believe to be transitional stages, have maintained that leukocytes with eosinophile granulation are derived from those with fine neutrophile granules. The transformation, they think, occurs either in the bone-marrow or in the circulating blood.

<sup>1</sup> From the Russian. Quoted by Ehrlich and Lazarus and others.

Loc. cit.

Loc. cit

<sup>4</sup> Journal of Physiology, 1896, vol. xix. p. 385.

<sup>5</sup> Arch. de biol., 1892, vol. xii. p. 199.

To many observers the number of eosinophile leukocytes in the circulating blood has seemed too small to explain the large accumulations not infrequently noted in various organs. Ehrlich, indeed, reached the conclusion that the eosinophile cells of the frog are, in part at least, transformed cells of connective tissue. The presence of eosinophile cells in certain skin lesions has suggested to Neusser and others that these cells in man may be formed in connective tissue. Certain writers, including von Leyden, Schmidt, and Grouven, who have studied the eosinophile cells in the sputum and blood of patients suffering with asthma, claim that they are formed in the bronchial mucosa. Stutz thinks that they may be formed in the intestinal mucosa as well. Howard and Perkins believe that eosinophile cells are formed in various organs, especially in the lymphoid tissue of the gastrointestinal mucosa and in various exudations, from lymphocytes and from plasma cells, and state that transitions from one to the other may be observed.

According to another view, the eosinophile granules are formed from material ingested by leukocytes. In many instances this belief has had its chief support in the fact that the material supposed to form eosinophile granules stains deeply with acid dyes. Klein<sup>7</sup> thinks that neutrophile leukocytes take up hæmoglobin derived from extravasated red blood corpuscles and are transformed into eosinophile cells; Sacharoff<sup>8</sup> holds a somewhat similar view. Tettenhamer<sup>9</sup> has described the formation of cosinophile cells in the degenerate testicle of the salamander; acidophile substance formed from nuclei undergoing degeneration is ingested by phagocytes. muscle infected with trichinæ T. R. Brown<sup>10</sup> found both neutrophile and eosinophile leukocytes in contact with the substance of much-altered muscle fibres. Finding, in addition, what he regarded as transitional stages between the two varieties of cell, he thought it probable that the neutrophile leucocytes form eosinophile granules by ingesting material derived from the degenerate muscle fibres. He supported this view by observations upon the relation of the eosinophile and neutrophile cells of the circulating blood. When with trichinosis the eosinophile cells in the blood were very greatly increased, the neutrophile leukocytes had undergone a corresponding diminution in number.

Metschnikoff<sup>11</sup> and Mesnil<sup>12</sup> also believe that eosinophile cells may be formed by a process of phagocytosis. Metschnikoff has seen spirilla of cholera ingested by leukocytes of the guinea-pig become so

<sup>&</sup>lt;sup>1</sup> Wiener klin. Woch., 1892, vol. v. pp. 41, 65.

<sup>&</sup>lt;sup>2</sup> Deutsche med. Woch., 1891, voi. xvii. p. 1085.

<sup>4</sup> Inaug. Diss., Bonn, 1895.

<sup>Johns Hopkins Hospital Reports, 1903, vol. x. p. 249.
Cent. f. innere Med., 1899, vol. xx. pp. 97, 121.</sup> 

<sup>8</sup> Cent. f. Bakt. u. Par., 1897, vol. xxi. p. 265. 9 Anat. Auz., 1893, vol. viii. p. 223.

<sup>10</sup> Journal of Experimental Medicine, 1898, vol. Ili. p. 315.

Annales de l'Institut Pasteur, 1894, vol. viil. p. 58.
12 Ibid., 1895, vol. ix. p. 301.

<sup>3</sup> Zeit. f. klin. Med., vol. xx.

<sup>&</sup>lt;sup>5</sup> Ibid.

altered that they stain readily with eosin, while Mcsnil maintains that anthrax bacilli are transformed into eosinophile granules by leukocytes of the lizard.

Summary and Conclusions. The opinions which have just been cited will not be discussed in detail. I will merely review certain facts which I believe serve to explain the origin of the eosinophile cells. In various tissues of the guinea-pig, notably in the mucosa of the gastrointestinal tract, in the mucosa of the air-passages, in the lymphatic tissue, and in the spleen, occur eosinophile leukocytes which are identical with those present in the circulating blood, and, like them, are provided with polymorphous nuclei. In the bone-marrow alone occur large mononuclear cells with cosinophile granulation. These cells of the bone-marrow undergo mitotic division and form daughter cells, which resemble in size the eosinophile leukocytes of the blood, while cells in which the nucleus presents varying irregularity in shape may be regarded as transitional forms. In the blood and in various organs the eosinophile cells give no evidence of multiplication.

The myelocytes with neutrophile or amphophile granules are analogous to the myelocytes with eosinophile granulation, resembling them in size and in the character of their nuclei. Muir¹ found that when the amphophile leukocytes in the blood of the rabbit undergo continued increase as the result of repeated bacterial infection, the myelocytes of the marrow are increased in number and mitotic division proceeds actively. An analogous phenomenon has been noted in those guinea-pigs of which the circulating blood contains a very large proportion of eosinophile leukocytes. The number of cosinophile cells is far greater than usual, while particularly abundant are the large eosinophile myelocytes. Mitotic division of these cells is observed much more readily than in the marrow of animals in which the blood contains few eosinophile leukocytes.

In certain instances in which eosinophile cells have accumulated in the tissues it has been possible to demonstrate their abundance in the bloodvessels of the part, and in one case the process of migration was actually demonstrable in sections of the hardened tissue. In apparently healthy guinea-pigs eosinophile leukocytes have been shown to migrate from the bloodvessels into the wall of a small bronchus, and hence through the epithelium into the lumen. Eosinophile cells manufactured in the bone-marrow reach the tissues by way of the bloodvessels.

The number of eosinophile cells in one cubic millimetre of blood is found to varŷ from day to day, and at intervals of three or four days undergoes an increase. It is not improbable that the number of eosinophile cells which the bone-marrow discharges into the circulation is subject to periodic variation. Complete withdrawal

<sup>&</sup>lt;sup>1</sup> Journal of Pathology and Bacteriology, 1901, vol. vii. p. 161.

of food is followed by a decrease both in the proportion and in the absolute number of eosinophile leukocytes in the peripheral circulation. Disturbance of nutrition acting doubtless on the bone-marrow affects the multiplication of the eosinophile cells more readily than that of the polynuclear leukocytes with fine granulation. Diminution in the number of eosinophile cells is preceded by a temporary increase, which may be explained by supposing that ripe eosinophile leukocytes already stored in the marrow reach the circulation, and, perhaps, are no longer diverted to the intestinal mucosa. With the administration of food the eosinophile cells of the blood gradually increase in number, but neither the weight of the animal nor the eosinophile leukocytes increase continuously. That there exists a close relation between the nutrition of the animal and the eosinophile cells is shown by the fact that variations in weight and in the number of eosinophile cells take with much regularity opposite directions, so that a temporary fall in weight is accompanied by a rapid increase of the eosinophile leukocytes, while a rise in weight tends to retard this increase.

## CIRCUMCORNEAL HYPERTROPHY (VERNAL CON-JUNCTIVITIS) IN THE NEGRO.

By Swan M. Burnett, M.D., Ph.D., • of washington, d. c.

IT would seem from a report of the discussion of a most carefully prepared paper on "Vernal Conjunctivitis," read by Dr. W. C. Posey¹ at the last meeting of the American Medical Association, at New Orleans, that opinion is far from being settled as to the peculiar manifestations of this singular affection in the negro in this country. As some statements of mine in a paper published in Knapp's Archives in 1881, in which the phases of the disease as it appears in the negro were first brought to the attention of the profession, have apparently not been clearly understood or not confirmed by other observers, it may not be without interest to revert to the subject again in an endeavor to harmonize views and clarify some seeming obscurities.

It appears to be a question with some whether the appearances described in that paper, and also in my chapter on "Diseases of the Conjunctiva" in Norris and Oliver's System, are not those of phlyctenular conjunctivitis, instead of that distinct form of disease now generally denominated as "spring catarrh" of the conjunctiva.

A rather extensive study of the disease (principally by Europeans) since Sämisch first reported upon it in 1876 has not added greatly to

<sup>&</sup>lt;sup>1</sup> Published in Journal of the American Medical Association, July 25, 1903.

our very limited knowledge of the cause and pathology of the affection. The clinical characteristics of that feature of the disease manifest on the globe are so distinctive that it seems quite impossible that anyone who has once seen a pronounced case could be mistaken in the diagnosis, so utterly unlike any other known condition is it. The above-mentioned opinion of some well-known and accurate observers that it may be a form of phlyctenular disease leads me to think that they have never seen a typical case of circumcorneal hypertrophy; from which we may infer that the affection is much more frequent in some sections than in others, a fact that may be found of no small etiological importance, and give a clue which should be assiduously followed up. Those of us whose work lies in localities where the negro abounds are well aware of the great frequency of scrofulous or strumous affections of the cornea and conjunctiva in that race, and can confirm Dr. Bruns' statement as to its frequent cause of blindness and greatly impaired vision. But there is no manifestation of this diathesis, either on the cornea or conjunctiva, which at any stage bears any resemblance to the ocular form of circumcorneal hypertrophy as found in the negro. The clinical features of scrofulous conjunctivitis are marked by certain constant and well-recognized characteristics. When it appears under the distinctly phlyctenular form the elevations are discrete, though they may be several in number. Whether the inflammatory symptoms are slight or severe, the natural history of the phlyctenula is the same; its wall bursts, its contents are discharged, and an ulcer results, which heals, as we know, with a very greatly varying rapidity. Photophobia and lacrymation are rarely absent, and may be present in the intensest degree. When the manifestation is on the cornea itself the exudate is still more or less circumscribed and small, with a very variable amount of destruction of tissue and cicatricial formation as a result. On the other hand, the distinguishing mark of circumcorneal hypertrophy is that it is not destructive. It is a true hyperplasia, and it was with a view of making this essential feature prominent and descriptive in nomenclature that I adopted the name "circumcorneal hypertrophy" as the best English synonym of the "hypertrophie perikeratique" of Desmarnes and the "gallertige Verdickung des Limbus" of Gräfe. This hyperplasic character of the pathological condition has been confirmed by all examinations of the tissue that have been made. Scheile has shown that the principal change in the circumcorneal form is in the epithelial layer, manifested by a largely increased number of the cells with invaginations, constituting the so-called "cancroid formations," together with some A drawing representing these increase in the connective tissue. appearances is given in my chapter on "Diseases of the Conjunctiva" in Norris and Oliver's System. Some more recent investigations made by de Schweinitz and Shumway, and published in the University of Pennsylvania Medical Bulletin for June, 1903, reveal identical changes in the conjunctiva of the lid. Everywhere there is

hypertrophy and nowhere a destruction of tissue.

There has not been a season since the publication of my paper in 1881 in which I have not observed cases of this disease—sometimes in considerable numbers—and not once have I observed any tendency toward destructive ulceration. If there is a destructive process, it is not circumcorneal hypertrophy. On the subsidence of the hypertrophy during the winter there seldom remains any sign of its former presence.

There are cases in which the symptoms of irritation are considerable. In the bulbar form, when the conjunctiva of the lid is but little involved, these symptoms are confined to a slight hyperæmia of the conjunctiva of the ball, but more often there is no complaint of photophobia or lacrymation. In the palpebral form, especially where there are large hard excrescences which rub on the cornea, the irritation may be quite marked, as indicated by a congested state of the conjunctiva of the globe and some photophobia. There is, however, never an involvement of the cornea aside from the hypertrophy. The usual, and, indeed, the characteristic complaint is not of pain, but of an intense itching of the eyes and sometimes of a "burning sensation," quite distinct from the subjective symptoms of phlyctenulæ.

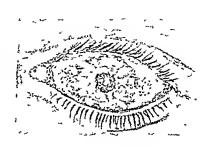
It is the objective appearance, however, which is so strikingly distinctive, especially in the bulbar form. The dirty gray elevations at the base of the cornea bear no resemblance whatever, when they are at all marked, to any other pathological condition found there. It must be remembered in this connection that the circumcorneal epithelial changes vary enormously in degree. Sometimes they are so slight as to escape detection unless carefully sought for. be that there is manifest only a macerated condition of the cells, with some slight increase in number, and confined to a very limited portion of the corneal circumference. Even in pronounced cases the hypertrophy may not go entirely around the cornea. I believe that in every case, even where the changes are supposed to be limited to the conjunctiva of the lid, a careful examination will reveal some changes at the limbus. I have one such case, in a negro girl, aged nine years, under observation at my clinic now, in which the palpebral changes in the form of granulations are typical, but the circumcorneal alterations could easily be overlooked if particular care were not given to finding them. This child has been subject to the disease since she was three years old, the symptoms beginning in March and continuing until October. In her the rubbing of the cornea by the granulations gives rise to some lacrymation, but the irritative symptoms are slight.

At other times the alterations around the cornea are so striking that when seen fully blown, for the first time in the negro, they are likely to confound even an experienced diagnostician in eye diseases. I remember such an experience with one of my associates in a hospital in this city. He was a man trained to careful observation, and had followed some large eye clinics in a neighboring city in the South, where the clientèle of negroes was large. He asked me to see a case of peculiar corneal disease, the exact nature of which he was unable to determine. As soon as the patient, a negro boy, aged eight years, entered the door of the clinic room I turned and asked him if he had ever seen such a condition before, recognizing, as I did, even at that distance, what the disease was. He was greatly surprised to find that it was a typical case of circumcorneal hypertrophy in the negro, a condition with which he was entirely unfamiliar, though he had seen the disease in the white race. Thereafter there was never any difficulty in his diagnostication of even slight forms of that disease, for it is a fact that one familiar with its appearances in the negro can easily make the diagnosis across the room. There is an aspect of the eyes, due to the peculiar appearance of the palpebral aperture, which, once seen, cannot be taken for anything else. The "white" of the eye in the negro, especially in the young, is very clearly marked, often brilliant, in contrast with the surrounding dark skin. In circumcorneal hypertrophy this is changed. The palpebral aperture has a dull, soggy look, and a dusky appearance, as though it had been smoked. This "smoked" look is not always of the same intensity, but even in mild cases is sufficiently pronounced to be recognized at a distance of many feet. In no other affection of the eyes in the negro have I encountered this singular look of the palpebral aperture. A closer examination shows the cause of this "smoked" appearance to be a pigmentation of the conjunctiva, which is more or less thickened and easily thrown into folds with the movements of the ball inward or outward. The epithelium has some of that lack-lustre look which is seen in a greater degree in xerosis of the The smoky look is confined almost entirely to the space exposed by the palpebral fissure. The parts usually covered by the lids are not affected. The pigment is usually in very small, dot-like points, to be differentiated only under a magnifier, but toward the base of the cornea it may be in quite large masses, some of which measure a quarter of a millimetre in diameter. This smoky look of the palpebral aperture disappears with the subsidence of the disease during the colder months, when the eyes return to approximately their normal appearance; not always, however, for there are occasional cases which continue, with all the characteristic appearances, during the winter months, though commonly with diminished intensity. The statistics at my clinic and also, I learn, from my confrères, at the other eye clinics in Washington, show that the negro in this section is much more prone to the disease than the white race. At my clinic it is rare to see a case among the white patients. Of thirteen cases of the disease recorded during the last eighteen months all were colored.

Opinions differ as to the relative frequency of the bulbar and palpebral forms. My own belief is that they both exist together, but one may be so slight as to escape detection unless carefully looked for. I also think that the same patient may have one or the other form more pronounced at different seasons.

A typical but extremely pronounced case of the disease in the negro is shown in the accompanying drawing. The patient was

a negro boy, not perhaps of full blood, but quite dark, who at the time the drawing was made (1899) was sixteen years old. The dull, "greasy," gray hypertrophy, which was elevated 0.5 mm. to 1 mm. above the surrounding tissue, was irregular as to surface, and not only occupied the conjunctival tissues in the vicinity of the cornea, but in-



vaded the corneal surface so far as to leave less than one-half of the iris exposed to view. Both the internal and external edges of the elevation were irregular in outline. The cornea inside the inner border was perfectly clear and the vision was not materially affected. The conjunctiva visible within the palpebral fissure was dark brownish in tinge, and there were many points of pigment in the vicinity of the elevation arranged, as they usually are, in the form of triangles, with their apices toward the canthi. The conjunctiva of the lids presented an appearance quite different from that usually seen in such cases, in so far as there was not that distinctly granular aspect which is commonly regarded as characteristic. The tissue was much thickened and lined with many furrows, undoubtedly an exaggeration of the same pathological changes that produce the excrescences—namely, a large proliferation of the epithelial structure. Both eyes were affected and practically to the same extent. The final issue of the case, which I followed for several years, I am not able to give, as the patient disappeared from view soon after the drawing was made.

That the disease is the manifestation of a dyscrasia scems certain, but it is not so certain what that dyscrasia is. Of course, we can never exclude what we call scrofula in any patient of the colored race, and yet there is nothing about the appearance of the condition itself or in the patients which would justify the acceptance of any such stigma as a cause. It occurs often in the most robust-looking, with none of the usual signs of deficient nutrition. I have looked in vain for some connection of inherited syphilis with the disease. In my experience the male and female sexes are about equally represented; and while principally an affection of childhood, the adult is by no means free. I have seen one pronounced case in a mulatto woman aged thirty years. Both eyes are

affected, but not always at the same time nor in the same degree. As is well known, the disease is most prevalent during the hot months, and so far as a seasonal nomenclature is applicable, "summer conjunctivitis" would be the more nearly appropriate. Strictly speaking, however, the affection is not a conjunctivitis at all, taking conjunctivitis to mean an inflammation of the conjunctiva. It is not only not confined to the conjunctival tissue proper, but there are none of the clinical characteristics of conjunctival inflammation, there being seldom any increase in the conjunctival secretion, either mucous or purulent. The term "catarrh" may be accepted in the conventional meaning of that term as applicable to all alterations in the mucous tissues.

The possible relation of the disease to trachoma has naturally attracted attention, since the granular condition of the lids suggests in some instances the appearances in trachoma. The similarity, however, is only superficial, for the essential nature of the two conditions is diametrically opposite. In trachoma the action is destructive, whereas in this disease it is purely hyperplastic, and when the affection subsides for the winter the conjunctiva assumes an almost if not quite normal appearance. There is an observation in this connection, however, which is not only interesting in itself, but may prove of value in making our final judgment as to the pathology of the disease, which should be noted, and this is the almost total absence of circumcorneal hypertrophy in Russia, where trachoma is so rampant. According to Natanson, the "flying column" of 100 oculists, which was sent throughout the provinces of Russia from 1893 to 1897 to look after diseases of the eye among the peasantry, did not meet among 168,618 patients, a large percentage of whom were trachomatous, with a single case of vernal conjunctivitis. Of course, it may be said that only the severely affected applied for treatment, and, circumcorneal hypertrophy being a practically painless disease, the stoical peasants paid no attention to it. But the reports from the clinics at St. Petersburg, Moscow, Kiew, and other Russian cities show the same practical immunity of the Russian from this affection.

This fact, taken in connection with the other fact that the negro in this country is practically immune from trachoma and is very liable to circumcorneal hypertrophy, offers a suggestion as to an antagonistic character in the diseases which, if followed up, might lead to some more definite knowledge of both affections. It would be instructive to know how such countries as Ireland and Southern Italy, as well as other localities where trachoma prevails, stand as to the percentage of circumcorneal hypertrophy. At any rate, these facts, as well as others, point most strongly to a racial influence, and a dyscrasic nature for both affections. Temperature, humidity, and

<sup>&</sup>lt;sup>1</sup> Klin. Monatsbl. f. Augenheilk., April, 1900.

elevation do not seem to be controlling factors to any great degree according to Natanson.

In regard to therapeutics, the indications, in view of what we know of the pathology, are for palliative local measures. Operative procedures, such as excision of the masses, expression, etc., have been recommended and practised, but evidently are not advisable. Attention to the nutrition and an improvement in the general condition are more properly called for. Arsenic administered in some form meets with the approval of most of those who have written upon the subject.

# A CASE OF SEBORRHŒA NIGRICANS (BLACK MASK OF THE FACE).

By Arthur Van Harlingen, M.D., of philadelphia.

I AM obliged to my friend Dr. J. S. Bethune, of Baddeck, C. B., for the opportunity of seeing this extraordinary affection of the skin and also for some notes of the history of the case.

Maggie McL., aged twenty-three years, comes of a neurotic family. Some members of the family are said to have suffered from mental alienation, and her father is a man of marked peculiarity of temper and disposition. Until her nineteenth year the patient enjoyed fair average health. She was brought up in the salubrious atmosphere of Cape Breton, but had lived out as a domestic, in Boston, I think, for a short time.

At this age she began to fail in health, although an exact statement of the symptoms could not be obtained. She was obliged to relinquish domestic service, returned home, took to her bed, and had remained there for four years up to the time of my examination. This scanty history was all that I could get of the patient's previous condition. It was, however, stated that soon after she took to bed a discoloration began to appear upon the face, which gradually spread and grew deeper in color until the entire visage was covered with a thick black mask.

Within the past few months the area of discoloration diminished until it had shrunken to the dimensions about to be noted. When I first saw her the patient was lying in bed in a small one-room cottage within a few feet of the cook-stove. She had been bedridden for several years, but, although somewhat emaciated, did not seem particularly ill. The limbs could be moved without much difficulty, though each movement and even a touch excited complaints of pain. She usually lay with her eyes shut, the lids twitching, and

seemed to be suffering from photophobia. The face was flushed and mottled, the skin dry and scaly. The lips were dry and the skin immediately circumjacent covered with a yellowish sordes or crust, vesicular or seborrheeic in character, which surrounded the whole mouth. Her tongue was parched, red, and slightly fissured. It was said that this eruption about the mouth was accustomed to run a course of several weeks, turning black and falling off, to be succeeded by a fresh outbreak. The forehead and nose were covered with a most extraordinary mask or crust more than a quarter of an inch thick, resembling a rind of ham—soft, greasy, sharply defined about the edges, and rounded. It could be easily broken off, and the forceps could be thrust into it at any point as if the crust were comprised of soft fat. The color of the crust was exteriorly of an inky blackness and tolerably smooth. The appearance of the face was as if a mask or vizard were worn over the upper part.

The patient's general condition was that of an hysterical person. The shrinking from light, the groans and complaints on the slightest



attempt at moving her, or even touching any part of the body, were highly characteristic. Trials at various points of the surface with a sharp object failed to disclose any areas of insensibility; in fact, the tactile sense appeared normal. Exception should be made of the scalp, which was certainly hyperesthetic.

She had complained for some weeks of extreme sore throat, but seemed able to swallow without much difficulty. It was said she had taken nothing in the way of food for some weeks, but

only an occasional drink of water. Her comparative lack of emaciation and the fact that the evacuations by the bludder and rectum were regular scemed to militate against the accuracy of this statement.

The attendants were supplied with a solution of sapo viridis in water and directed to endeavor to loosen the mask by daily washings. At the end of a week, however, when I saw her for the second time, the mask had not been at all cleaned off. It was loosened, however, and I had no difficulty in stripping off the entire coating. It came away like a thick crust of fat, tearing here and there, where undue traction was made. The outer surface was smooth, rather dry, and black, with bits of wool, hair, etc., matted in it. The internal surface was of a whitish color, soft and very greasy, showing numerous conical elevations, corresponding to the openings of the glands. The skin underneath was washed clean of the mask-coating, and then

appeared moist and oily, the epidermis rather sodden and in places slightly abraded. The process of removal was in no way painful. The parts affected were ordered to be washed daily with a watery solution of green soap and powdered with a mixture of aristol and boric acid. A week after this I saw the patient again for the last time. The skin of the face was dry, red, and slightly scaly, the powder having dried it off. The washing having been very imperfectly performed, some greasy patches were still left of the mask. Also along one side of the nose there was a greenish crust, evidently seborrhæic in character. The skin being abnormally dry, it was decided that while continuing the daily washing with soap and water a dilute oxide of zinc ointment should also be employed. I preserved a portion of the greasy mask-like crust, which dried up gradually and shrunk, but retained a most offensive odor. Treated with ether a portion of the crust separated into various and heterogeneous components; there were fragments of wool and hair, granular débris, probably dust and grime, and whitish soft bits of tissue, which, picked out, treated with a solution of eaustic potash and glycerin and examined under the microscope, were found to be composed of epithelial seales, with fine granular oil globules. The epithelial seales seemed dry and were not in a state of fatty degeneration. There were some few lanugo hairs.

The eonelusion reached was that we had to deal in this ease with a severe case of oily seborrhea, giving rise to a dusky secretion upon the surface, which had been allowed to accumulate for several years, and which had, perhaps, been added to by the inunction or application of ointments and dressings of various kinds, together with accretions from the surrounding apartment, dust, flakes of soot, the sweepings of the carpet, etc. Most patients suffering from such affections are cleansed more or less frequently, and it is only by long-continued neglect that such extraordinary results are reached.

We have become familiar of late years with that form of chromidrosis which occurs in a black circle about the orbit or in rarer cases upon the forehead of certain hysterical women. In these cases the oily secretion from the coil glands is changed in color and consistency, and forms the discolored crust. In some cases, however, the sebaceous glands play the most prominent part, and such, I think has occurred in the case reported. As I believe this to be unique, I have not given any reference to the cases of chromidrosis recorded. A complete account of the latter affection is given in my article in the Twenticth Century Practice of Medicinc, vol. v. p. 539, where the symptoms are fully described.

<sup>1</sup> Since these notes were written I have received a letter from Dr. Bethune. He says: "The patient complains of a great deal of pain all over the face and head. The skin in patches over the face looks very red. She says it burns. This very likely is caused by the too frequent use of the sape viridis, so I ordered it used less frequently. There is no sign of the mask, nor is there any schaceous matter about the sides of the ala nasi. Her general condition is about the same as when you saw her (three months ago)."

## A REPORT OF TWO CASES OF ECTOPIC GESTATION AND A CASE OF INTESTINAL OBSTRUCTION DUE TO MECKEL'S DIVERTICULUM.

BY HAROLD H. HEYER, M.D.,

AND
H. M. LEE, M.D.,

OF NEW LONDON, CONK.

Case I.—Mrs. X., white, American, aged twenty-six years; married in June, 1902. Housewife by occupation, presented herself at the office of my colleague, Dr. Heyer, on May 6, 1903, complaining of what she considered a prolonged menstrual period, and also of some slight pain and tenderness in the lower abdominal region

Family History. Negative.

Personal History. Had never had any illness she could remember except an attack of peritonitis (so-called) when eleven years of age.

Menstrual History. Commenced menstruation at the age of twelve years, and except on a few occasions had menstruated regularly. The average duration of her periods was five days—menstruating at an interval of twenty-eight days.

Since marriage her menstrual periods have appeared with regu-

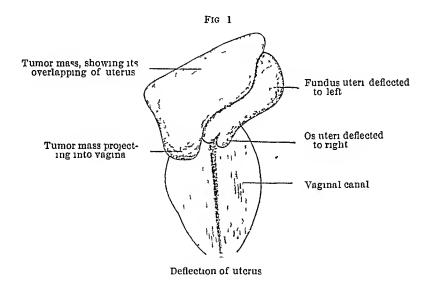
larity and without pain. She had never been pregnant.

Present History. On April 18th the patient was exposed to cold and wet, being alarmed thereby, because she expected her menstrual period to appear on April 19th. This, however, did not occur until April 22d, hence was delayed three days. From this time, namely, April 22d, to time she sought counsel, May 6th, she had flowed irregularly, the flow appearing suddenly and copiously at times, with some clots and of a dark color; then abating from a few hours to a few days. Pain, referred to the lower right abdominal region, and at times radiating downward over the anterior surface of the thigh, accompanied these periods of flowing. On several occasions faintness was marked. The patient was about during this time. The above irregular discharge and general condition continued up to May 12th, when she again consulted Dr. Heyer, her family physician. The patient was ordered to bed to insure rest and quiet, and, abortion being suspected, examination per vagina was made, with negative evidence. No sign or symptom of pregnancy could be adduced by a general physical examination. Throughout the whole vaginal vault tenderness was elicited upon pressure, more particularly on the left side. No tumor mass was detected, in fact, except for tenderness, this careful general examination was entirely negative. With conditions as above stated the patient remained in bed for the most part, when, during the night of May 19th she was seized

with a very sudden sharp pain in the lower right abdominal region, accompanied by faintness and nausea. In the afternoon of May 20th Dr. Heyer was summoned, and upon examination a tumor was discovered occupying the lower right abdominal region. I was requested to see the patient in consultation, and at 6 P.M. found the following condition to exist:

The patient was in bed lying upon her back, with knees drawn up. Expression anxious and face pinched. Paleness of mucous surfaces quite marked. Mind clear and mental faculties fully acting. Temperature, 99.5° F.; pulse, 100, regular in rhythm, but irregular in volume, soft, small, rather pronounced upstroke. Respirations 30, shallow and thoracic in character. The patient complained of a tense dull pain in lower part of abdomen; slight headache; faintness, and no appetite. Thirst was not marked.

Physical Examination. Chest: Lungs normal. Heart rapid, regular, decreased muscular sound; valvular sounds normal.



Abdomen: Inspection, slight rigidity of right rectus muscle and some bulging in lower right abdominal region apparent on deep inspiration. Otherwise negative.

Palpation. Above a line corresponding to the umbilicus palpation

Palpation. Above a line corresponding to the umbilicus palpation revealed no abnormal condition. Below this line tenderness was manifest generally, but more severe in the lower portion of the abdomen from the mesial line outward to a point corresponding to the junction of the outer and middle thirds of Poupart's ligament, and extending upward toward the umbilicus.

Pain on pressure was intense over this area, and produced faintness. A tumor was readily detected. The tumor mass was resistant and firm, the outer and upper border being sharply outlined.

Percussion. The percussion note over the various regions of the abdomen was normal, except over the tumor mass, where a dull note was elicited.

FIG. 2.

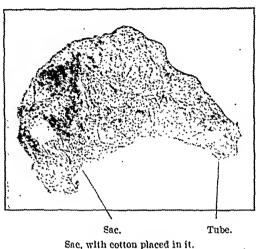


Fig. 3.



Other side of tube. Extent to which ovary was encroached upon in the sac formation. 1, 2, 3. Membrane and villi.

Vaginal Examination. The examining finger at once encountered a tumor mass projecting downward into the right side of

vaginal canal, reaching below the cervix. The cervix was soft, and the os slightly dilated, discharging a dark bloody flux. Intense pain was elicited upon pressure throughout the vaginal vault. Cervix directed toward the right side. (See Fig. 3.)

Bimanual Examinations. Fundus of uterus deflected toward the left side. (See Fig. 3.) Uterus very slightly movable and perceptibly enlarged. Left ovary and tube readily felt and apparently of normal size. The tumor mass was very tense, immovable, and its upper borders sharply defined. The inner border seemed to merge into the body of the uterus and embrace that organ. (See Fig. 3.) However, it was apparent that there was no direct connection between the tumor and the uterus. This mass filled the pelvis on that side and was triangular in outline (see Fig. 2), extending upward in the mesial line two-thirds the distance from the symphysis pubis to the umbilicus and outward to a point corresponding to the junction of the outer and middle third of Poupart's ligament.

The right ovary and tube could not be made out. A dark thick discharge filled the os, and blood clots were quite numerous in the vagina. Examination of this discharge failed to reveal any membrane. During the examination the patient complained of increased

pain throughout the entire pelvic cavity.

A diagnosis of rupture of an ectopic gestation sac was made, and operative interference was advised at once. The patient was admitted to the hospital on May 21st, and I operated on her the

afternoon of that day.

On examination of the pelvic cavity it was found that the rupture of the gestation sac had taken place into the broad ligament, and dissected along between the layers of that structure close up to the body of the uterus. The reason of blood escaping as the peritoneal cavity was entered is explained by the fact that I either opened the wall of the hæmatoma, or else from the pressure alone it ruptured. The tube and ovary were now extirpated, and one litre of salt solution put into the cavity of the abdomen and the wound sutured in layer except at the lower inch, through which gauze drains were placed. The patient withstood the operation well, and her recovery was uneventful. Primary union was obtained and the drainage removed on the third day. At the end of two weeks the patient was allowed the liberty of moving about in bed, and on the sixteenth day, a tight-fitting support being applied to the abdomen, she sat up. At the end of three weeks she was discharged from the hospital.

Examination of the extirpated tube and ovary shows the gestation to have been of the so-called tubo-ovarian variety. It seems to me quite remarkable that this variety of ectopic gestation should have

ruptured into the broad ligament. (See Fig. 2.)

The sac occupied quite a portion of the ovarian tissue, as shown

in Fig. 3, which also shows the fetal membrane in part.

HEYER, LEE: ECTOPIC GESTATION. At the present writing the patient is enjoying as good health as ever, and the only discomfort from her serious difficulty and severe ordeal is a feeling of stiffness in the right groin, only evident after

indulging in rather excessive exercise, and on becoming fatigued. However, the patient tells me that this feeling is gradually disappearing. CASE II. Mrs. Y., aged twenty-nine years; weight, 119 pounds; height, five feet two inches; American born of Scotch descent. Was married in June, 1898; housewife by occupation; was never pregnant. Personal History. As a child was not particularly strong. Never

had any severe illness except an attack of diphtheria six years ago, and was not in her usual health for about a year thereafter. Mensirual History. The patient commenced menstruating at the age of twelve years, and so far as she can remember was regular, and did not suffer at these times. The usual interval between the periods was twenty-five days, and the periods, as a rule, lasted five penous was twenty-uve days, and the penous, as a rule, lasted fine normal course of her marriage there was no interference in days. For three years after marriage there was no interference in the normal course of her menstrual history, but for the past two years she had suffered pain at these times on the first and second

This painful menstruation increased in severity as time went on, and in March, 1903, the patient consulted her family physician with Dr. H. W. Nichols, of Brooklyn, he told me that he found with Dr. H. W. Nichols, of Brooklyn, he told me that he found Mrs. Y. had a retroflexed and retroverted uterus. The patient was under his care about three months, and was then discharged, her trouble having been overcome, and the parts maintained in normal relations by a pessary. dysmenorrhoea abated. I saw the patient for the first time on July 4th, and found her in During the time under treatment the bed suffering from pain in the lower abdominal region. At this time the patient's temperature was normal, pulse 80, and respiration of pain which che She did not feel sick, and only complained of pain which she described as being sliarp and not constant. This pain was assumed to the fact that che was monetriating by the patient to be due to the fact that she was menstruating.

Indicate the patient of the fact that she was menstruating. Inquiry into this menstrual period elicited the following facts: The patient menstruated on May 11th, the correct date for that function patient mensituated on Aviay 11th, the correct date for mai function she did not manetunate again until land 10th, and then only land 10th, and then only land a she did not menstruate again until June 19th, and then only had a She the the not mensituate again until June 19th, and then only had a ranged hyposis. This climbs discharge least un musti June 25th, on Panied by Pain. This slight discharge kept up until June 25th, on Pamen by Pam. Luis sugar assenting kept up unin sume zour, on the lower left abdon-Which day she was selzed with intense pain in the lower left abdomnall region, and became faint at the same time. She was comnall for a fam house mill the pain and faintness pelled to remain in bed for a few hours until the pain and faintness pened to remain in sed for a few dours unin the pain and remained in remained in a series and a sound again as well as ever. The slight flow continued irregularly until June 28th, when pain and

faintness again came on, but this time was only transitory. From this time until July 3d she was free from pain, and enjoyed her usual health. The slight flow continued, however, during this time.

On July 3d, in the night, after an active day, the pain came on again with great intensity, and I saw the patient at 6 A.M. July 4th.

Physical Examination. Chest negative. Abdomen: Inspection negative. Percussion note normal over the various regions of the abdomen, but elicited tenderness over the left lower abdominal region. On palpation tenderness was evidenced in the lower abdominal region over the uterus and its appendages, especially marked on the left side. No tumor mass could be made out.

Bimanual Examination. The pessary was removed, causing sharp pain. Cervix soft and slightly dilated. Uterus soft, movable, and enlarged perceptibly. The right tube and ovary easily felt and apparently normal. The left ovary apparently normal in size. The left tube was enlarged to about the size of a hen's egg, very tender, tense, and pulsating. This tumor mass was slightly movable and not directly connected to the uterus. Pressure about the vaginal vault elicited tenderness and caused severe pain. There was a rather foul odor to the discharge, which was dark in color and contained many clots. No membrane could be found, though the flux was carefully examined for such.

I strongly suspected I had a case of ectopic gestation, and explained to the patient's friends that operation was the best procedure, and advised the same. Under the circumstances, however, it was reasonable perhaps to have such advice received dubiously, and I was forced to leave the patient, with orders to remain in bed, to be quiet, and confine herself to liquid diet.

Owing to the press of other work I did not see the patient again until 8 P.M. At that time she was in intense pain and had been so for several hours.

Repeating my advice for operation, I summoned counsel, and at 10 p.m. Dr. Heyer and I returned to the patient. Her condition was most serious. She was not in pain, but anxious and very restless, and showed marked evidence of profound hemorrhage. Pulse 148, small, irregular, both in force and volume. Respiration 36, shallow. The thermometer did not register. The mucous surfaces were exceedingly pale, patient gasping and unable to speak aloud, complaining of suffocation, and asking for more air. Skin dry and cold. Heart very rapid and first sound exceedingly weak. Inspection, palpation, and percussion of the abdomen negative.

Strychnine and nitroglycerin were used subcutaneously; large amounts of normal salt solution introduced into the rectum, and hot applications externally. Without any means at hand for opening the abdomen we continued symptomatic treatment, and the patient

began to respond slowly.

Operation was now demanded, but with no one at hand who had the power to give consent to such procedure, and expecting the arrival of the patient's physician at any time, I could only continue measures against shock and hemorrhage.

Upon the arrival of Dr. H. W. Nichols, of Brooklyn, we found the patient in much better condition. Temperature 100°, pulse

120, very weak and irregular. Respiration, 30.

The patient was removed to the hospital, and I operated upon her, opening the abdomen in the median line from the umbilicus to the pubes.

Upon entering the peritoneal cavity a great amount of fluid blood

and blood clots escaped.

The tube was quickly found, tied off with a silk ligature, and extirpated. Search for fresh hemorrhage was made but none found. The abdomen was cleansed of the contained blood by flooding with normal salt solution in great amounts until it returned comparatively clear. The cavity was now partially dried, and search for the ovary made. This organ was found on the posterior surface of the broad ligament, and extirpated. The other pelvic organs were in good condition apparently. One litre of normal saline solution was now run into the abdominal cavity slowly, drainage established, and the wound closed by suture in layers. The patient acted fairly well under the anæsthetic, except on two occasions, when she became very weak. However, she left the table in far better condition than when I commenced the operation. Large amounts of saline solution were introduced per rectum, and this was kept up for thirty-six hours, almost all of it being retained, its administration taking place every four to six hours. The beneficial effect of this was very gratifying indeed. On the fourth day after operation the patient developed a sympathetic inflammation of the left parotid gland. No attention was paid to this, except wet dressings of a 5 per cent. solution of aluminum acetate were applied, and the inflammation disappeared in two days. Liquid foods were given in small doses frequently, as the stomach would allow, and champagne, brandy, with carbonated water, were given freely. Though these liquids were given very soon after the patient was returned to her room, yet they were borne exceedingly well and seemed to do much good. The patient made speedy progress toward recovery.

On the fourteenth day after operation, the wound having united throughout, she was allowed the liberty of moving about in bed, and on the eighteenth day she was sitting up in a wheel chair. At the end of three weeks the patient was up and about, a tight-fitting belt being used to support the abdominal wall. At the present writing the patient is practically a well woman, feeling in good health and showing only some anæmia, which is fast disappear-

ing.

Examination of the tube shows this to have been a true tubal

pregnancy.

The tube shows gross evidence of pathological change, it being thickened and tortuous, and a small cyst appeared at the extremity nearest the uterus. (See Figs. 4, 5 and 6). These are photographs of the tube and ovary, showing the gestation sac and point of rupture.

Fig. 4. FIG. 5. Sac.

Ovary and tube, showing sac and point of rupture.

Same as Fig. 4, with tube turned to side, showing size of gestation sac.

CASE III. A Case of Intestinal Obstruction due to Meekel's Diverticulum.—Infant A., male, aged seven months; white, American. Father and mother living and in good health. No family history of tubercular disease nor of any abnormal growths or deformities.

Mother had no difficulty with this the first child. Child breastfed, never had any other food but mother's milk until six months old, then had been given water freely and dry bread-crusts occasionally, but apparently never swallowed any amount of bread. Since birth the child had suffered from constipation at times, but had never had an attack of diarrhoea. The child had been under the care of two physicians at its home in Philadelphia for what seemingly were attacks of constipation. The child's bowels moved naturally twice daily on an average. However, a day or two before these attacks, which grew more frequent from birth until one week was the rule, the child's bowels would not move copiously as was the custom, and only once in twenty-four or thirty-six hours.

Fig. 6.



Other side of tube, showing sac protruding; also eystic portion of tube. A. Cyst.

Then the attacks of constipation came on, never lasting over thirty-six to seventy-two hours. The mother noticed that the movements were not at any time hard, but rather soft, and always free from undigested food.

Pain seemed to be the first evidence of trouble, and the child would cry out from time to time, drawing up its knees and straining quite violently without result. If the attacks lasted some few hours, vomiting occurred, generally of a bilious character. No temperature accompanied these The child would lie attacks. quiet when free from pain, oftentimes showing a desire for food. These attacks have never lasted over forty-eight hours, and the termination was signified by a movement of the bowels, never constipated in character, giving a very evident relief to the child, which seemed as well as ever as soon as the bowels moved. Such is the history I obtained from the mother on the day of my first Her physicians had exvisit.

amined the child often during these attacks, but evidently found nothing to account for this condition. The mother was advised not to feed the child at these times, except giving it water and small, frequent doses of some liquid food. Castor oil and a laxative tablet were used as a purge, and injections of hot water administered two or three times daily. Under such care the child had always recovered from these attacks, apparently none the worse for such experience.

The child arrived in this city on June 25th, with the father and mother, for the summer, coming from Philadelphia. At the begin-

ning of the trip the child was well, but during the ride on the train became somewhat fretful and cross, acting in the same manner as it had always done previous to one of these attacks of constipation. The bowels had not moved throughout that day until after its arrival in this city, when a very small movement occurred, accompanied by pain and considerable straining. The movement was soft in consistency and contained no undigested particles.

Throughout the night of the 25th the child was comfortable, and the bowels not moving on the morning of the 26th, the mother used the laxative tablet and enema without result. Throughout the day and night of the 26th the bowels did not move and the child lay quiet, taking little notice of surroundings, crying out with pain from time to time, and straining violently. The morning of the 27th there was no change, and vomiting of a bilious character

began. The mother again used enemas, without result.

I was summoned to see the child at noon of the 27th, and found the following conditions to exist: Child well nourished and nicely proportioned, lying upon its back with legs extended. No temperature. Pulse 130, good quality. Respiration a little quickened. Examination of chest negative. Examination of abdomen: On inspection abdomen flat, no distention, no rigidity. Abdominal respiratory movement evident. Palpation: Abdomen flaccid, no point of tenderness, no pain caused by examination.

Low down in the abdomen, evidently in the sigmoid, a mass about the size of a pigeon egg was detected, giving the sense to the touch of fecal matter. Throughout the rest of the abdomen palpation was negative. The percussion note was normal throughout the various regions of the abdomen. Examination by rectum revealed nothing. The tongue was slightly coated and the vomitus

without any odor.

With the history of the case as above written I felt that I was probably dealing with a case of temporary obstruction due to fecal matter in an abnormally long sigmoid flexure. Such was the diagnosis, and a high enema of oil followed by water was used without any result except a discharge of mucus and gas. The child was kept quiet, and egg albumen in water with small amounts of brandy given hourly. The mother was instructed to give enema of oil and glycerin every four hours.

The child remained in this condition without any change through-

out the rest of the day.

At 8.30 in the evening I again saw the child, and found upon examination no change in any respect. The child was quiet except when crying out with abdominal pain. I next saw the patient the following day at noon, and found the child had had no movement of the bowels and also was decidedly sick, lying in a somewhat stupid condition, but easily aroused; on examining the abdomen a tumor mass of intense firmness was found lying in the mesial

line between the umbilicus and the pubes, the long axis inclined from above downward and to the left.

This mass was about the size of a hen's egg, and the percussion note over it dull.

Realizing the gravity of the situation and fearing a permanent obstruction had taken place I requested counsel.

At 1 P.M. Doctor Heyer and myself found the patient in this same stupid condition, and at this time the tumor mass described had increased in size to that of a small orange, was evident on inspection, easily palpated, movable, and dull on percussion.

Believing a volvulus had occurred, about a quart of oil and glycerin was run into the rectum slowly. No result upon the tumor mass was made, and no gas or fecal matter escaped. There was no peristaltic movement felt or seen to take place around the tumor mass. The child was vomiting greenish fluid in small quantities frequently at this time. About one-half hour after using the high enema, while we were watching the abdomen, the child gave a sharp cry, and immediately we saw swelling take place over the site of the tumor mass described, which increased in size steadily until it was as large as a large orange and bulged forward to a considerable extent.

Upon laying my hand over this tumor the peristaltic movements of the intestine could be felt, and upon percussion a distinct tympanitic note was heard. Operation was advised immediately, and the

patient was taken to the hospital.

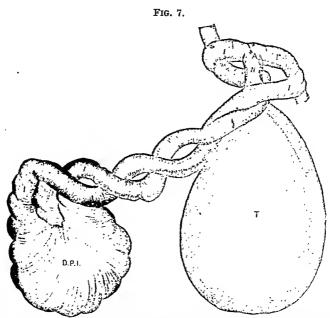
When seen at the end of another hour the child was vomiting fecal matter very often and seemed in a moribund state, temperature subnormal, thermometer in the rectum did not register. Respirations 40. Pulse very rapid and weak. The tumor mass appeared no larger to the eye, but on palpation a perceptible increase in size was evident.

Operation. The abdomen was entered by an incision in the median line from the umbilicus to the pubes. Upon opening the peritoneal cavity a white, glistening mass was seen lying against the abdominal wall, looking much like a distended portion of the intestine. On putting the fingers into the cavity this mass was pushed aside and the fingers swept about it. No adhesions being encountered, the mass was delivered from the cavity of the abdomen and with it a large proportion of the intestinal tract. This tumor mass was pear-shaped, about six inches in length, and some three and one-half inches across in the largest portion, firm to the touch and distended with fluid. (See Fig. 7.)

The wall was smooth and shining and covered with distended veins of large size. It was absolutely free from adhesions and was connected to the under surface of the ileum, some sixteen inches from the ileocolic junction, by its upper and smaller extremity through the medium of loose connective tissue for about three-

quarters of an inch. (See Fig. 7.)

The ileum had looped itself around the upper extremity of the tumor, and was then turned four times upon itself from left to right around the tumor mass, leaving a loop of gut some six inches long free and distended enormously with gas.



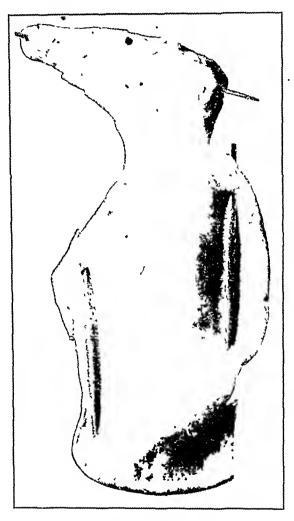
Tumor mass and volvulus. Sixteen inches from ileocolic junction. A. Attachment of tumor to ileum. D.P.I. Distended portion of ileum. I. Ileum. K. Neck of tumor. T. Tumor mass,  $6 \times 3\%$  inches.

The volvulus was reduced without difficulty. An incision was then made into the tumor mass, and some eight or ten ounces of a clear serous fluid escaped. The incision was now carried along the tumor down to its attachment to the intestine, and, no communication being detected between the cavity of the cyst and the intestine, the wall of the cyst was excised close to the gut. On account of the exceedingly precarious condition of the patient no time could be given to dissecting the tumor from the gut. The gut was in good condition, and circulation was well established in a few minutes by the use of hot towels. The gut as it was returned was run through the hand as a matter of precaution; incidentally the appendix which was abnormally long, was removed and the wound closed. The operation occupied some fifteen minutes. The patient rallied well from the operation, the fecal vomiting ceased, the bowels moved freely, and large amounts of gas escaped per rectum.

The aspect of the patient improved remarkably in a few hours. Though the operation was followed by almost unlooked for relief in every particular, yet no hope was entertained for recovery, and about ten hours after operation, as the child was moved upon its

pillow, it suddenly collapsed and died in a few minutes thereafter. Examination of the wall of this tumor mass showed it to be of intense toughness and very elastic, about one-eighth of an inch in thickness. (See Fig. 8.)

TIG S.



Wall of tumor mass

The neck of the sac presented grooves from the pressure of the intestine as they were twisted about it. This tumor was suspected to be an intestinal diverticulum, possibly Meckel's, and the report of the pathologist to the Hartford Hospital, Hartford, Conn., prooves it to be such.

Dr. Walter R. Steiner, Pathologist to the Hartford Hospital, Hartford, Conn., furnished me with the following pathological report of the case: The tissue coming from the wall of a cyst connected with the intestine was hardened in graded alcohols, embedded in celloidin, and the sections when cut were stained in hæmatoxylin and eosin.

The specimens on cross-section are seen to be composed of four layers or coats. The inner layer is made up of fibroelastic tissue, loosely compacted together and containing bloodvessels and lymphatics. In places there is a considerable amount of round-cell infiltration, especially about the bloodvessels. The next two layers are composed of muscular tissue—an inner circular layer and an outer longitudinal layer. The inner (circular) layer is the more compact of the two. The last or outer layer is fibrous in character and fairly vascular.

Diagnosis. From the location of the specimen and its structure (as seen on section), it seems probable that the cyst owes its existence to an intestinal diverticulum, which subsequently did not communicate directly with the intestine, but remained connected with it by adhesion (pedicle). The coats of the cyst correspond to the submucosa, the two muscular coats and the serosa, of the intestine. There are, however, no evidences of a mucosa. The location of the cyst with reference to the cæcum suggests strongly the possibility that it is a Meckel diverticulum.

The enormous size of this process in this case led me to make the above report, for I have been unable to find the history of its parallel. To theorize, perhaps, concerning this tumor mass we might say in the first place that it seems most plausible that the attacks of so-called constipation were in reality referable to this diverticulum, possibly by a temporary looping of the gut about it

or by pressure of the structure upon a portion of the gut.

I cannot believe in the face of the history of the case and after the careful examination of the abdomen, made by several physicians in the course of the infant's life, that such a tumor of the size described could have existed all this time without detection. And again, as I have already stated, the tumor I felt on June 28th steadily grew in proportions, making one strongly incline to the theory that by a constriction at the neck of the tumor a passive congestion took place and serum continually escaped from the very numerous vessels in the wall of the cyst, causing the tumor to enlarge. That the volvulus was of short duration, I am positive, for I could almost see it develop, so to speak. A post-mortem could not be obtained, but I have every reason to believe that the contents of the abdomen were in good condition after operation, and that shock was probably the chief factor in the cause of death.

The enormous size of Meckel's diverticulum and the interest which surrounds the life-history of this little patient, evidently referable to that structure, and the rarity of ectopic gestation have

led me to report these cases to my colleagues.

I am sure we may truthfully say that three desperate cases con-

fronted us, two of which are able to pay their tribute to the art of surgery.

I want to call attention to the use of saline solution in the peritoneal cavity as a means of counteracting shock and supplying the

body with fluid material.

In these two cases of ectopic gestation both patients had lost a great amount of blood, one being nearly exsanguinated. Upon the table both cases became in desperate condition, one particularly so. The opening of the peritoneal cavity, though occupying perhaps two minutes, with the loss of the contained blood, impressed both patients very markedly, but very soon after the saline solution was run in the peritoneal cavity—and this was the next step in the operation after securing the tube by ligature—the beneficial effect was observed both in the circulation and in the general appearance of the patient. In fact, it was not perceptibly longer than has been the case where I have used salines intravenously. was the good result that the patients in both instances were kept upon the table some forty or fifty minutes, whereas the operation could have been completed in fifteen or twenty minutes. This solution was not only absorbed rapidly, but its effect was most marked, and it cleansed the cavity effectually, doing away with having to use so foreign a substance as the operator's hands or instruments among the intestines and against so sensitive a membrane as the Also the edges of the wound were insured against injury.

A rather significant fact is this: that no atony of the intestinal

tract followed these operations.

In the case of the infant the beneficial effect of the saline, though used, was not so noticeable; but here no loss of blood had occurred. I feel certain, however, that the element of shock was at least mitigated. We know the peritoneum has a most wonderful capacity for absorption, and my experience in these and other cases has led me to use the abdominal method of administering salines in cases of abdominal surgery, where from loss of blood or from shock such would be indicated.

A case of double ovariotomy illustrates this practice well. The patient lost no blood, but owing to adhesions I had spent some thirty minutes before I could extirpate the tubes and ovaries. About this time the patient showed marked evidence of shock and collapse. I ceased further manipulation, and ran into the peritoneal cavity some three pints of salt solution. It was only a short time when the patient rallied, her pulse came up, and the operation was then completed without any further difficulty. She made an uneventful recovery. Owing to oversight on the part of a nurse no stimulation was at hand, and when ready was not needed.

### LUDWIG'S ANGINA

REPORT OF A CASE.

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Ludwig's angina is an infectious inflammation of the cellular tissue in the floor of the mouth, beneath the jaw, also behind it and down the neck as far often as the clavicle and sternum. The following case illustrates its pathology and treatment. It is often fatal.

C. R., male, aged twenty years, had had a bad tooth in the lower jaw, right side, for some time. A week previously the neck began to swell and later rapidly increased, until on admission he was only able to part the jaws less than a centimetre; the tongue was thick and filled the mouth, and it was also pushed upward by the swelling on the floor of the mouth. The neck was enormously swollen, the swelling extending from the zygoma above to the clavicle and sternum below, and from the edge of the trapezius muscle on one side to beyond the median line on the other. He had stertorous breathing, difficulty in swallowing, and could only talk in a whisper. Under primary anæsthesia an incision was made in the line of the anterior edge of the sternomastoid muscle and two rubber drainage-tubes passed parallel to the jaw and brought out near the median line. Only a very small amount—a few drops—of pus was obtained. The temperature was 101° F.; pulse 120; respiration 24.

The case is interesting for several reasons. The photograph, which was taken about the second or third day after operation, shows the swelling extending up to the zygoma. The swelling around the lower part of the neck is not shown, having disappeared, owing

to the drainage.

The fact that the patient could only speak in a whisper and the noisy respiration showed that there was cedema of the larynx and probably compression of the trachea. That the cesophagus was compressed was shown by the trouble in swallowing. The greatest swelling was between the jaw and the clavicle. Immediate relief was required. While there was a feeling of fluctuation, no collection of liquid was found on operating. It was decided to place the incision some distance below the angle of the jaw, so as to avoid any superficial veins, for there is not infrequently a communication between the external and internal jugulars at this point, or the temporomaxillary and facial veins may there be encountered. As soon as the deep fascia was opened a closed hæmostat was pushed ahead into the tissues and opened. In this way two passages were tunnelled upward to beneath the lower jaw; also two across the neck, one curving upward toward the jaw and the other downward toward

the clavicle and sternum. Drainage-tubes were placed in each. No distinct collection of pus was found. The tubes were surrounded with gauze. A culture showed an unmixed growth of virulent streptococci. The symptoms improved slightly by the next day, but not to the extent desired, and as there was practically no discharge from the tubes, the gauze dressing was removed and substituted by a flax-seed poultice. I thought that any further infection could only be for the better, and the poultice, I felt sure, would hasten and favor reso-



lution. This it apparently did, for the next day the discharge of pus began, and the temperature had reached normal. On the fifth day after operation the discharge of pus was more free and the patient was taking solid food. He was dismissed on the tenth day, with the discharge almost stopped, and his general and local conditions excellent.

Some authors regard the disease as resembling erysipelas. This seems to me to be so only to a small extent. I believe it to be a distinctly local condition, propagated by travelling by direct continuity of tissue and capable of being relieved by free opening of the infected area. The safest way of making this opening is by pushing the nose of a hæmostatic forceps carefully into

the tissue and opening the blades and so working one's way onward. The large bloodvessels of the neck did not appear to be pushed up near the surface by the effusion, but lay probably close to their normal position posteriorly. There was a direct causal relation between the diseased teeth and the onset of the inflammation. This fact, together with the prompt subsidence of both local and constitutional symptoms, as the result of local treatment alone, all point to the disease as being a distinct local infection and not erysipelatous in character. Complete anæsthesia is dangerous in these cases, and the safest course would be to use local anæsthesia or none. In this case it was simply used to deaden the skin incision.

## A FATAL CASE OF POISONING WITH OIL OF GAULTHERIA.

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AND

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F F

The rarity of cases of fatal poisoning with oil of gaultheria makes the case we are about to report of some interest. It occurred at the Polyclinic Hospital in the service of Dr. McKee, through whose courtesy we are enabled to report it.

The patient, Fannie H., a child, aged two years, was brought to the hospital about 9.30 A.M., on April 18, 1903, by its mother, who said that it had swallowed the contents of a bottle, which she brought with her. As the bottle had been bought by the patient's father at the pharmacy in the hospital, it was easy to determine that it contained commercial oil of wintergreen, which is in reality oil of birch. It was estimated that the child had taken a drachm of the drug. The child had vomited several times before being brought to the hospital, and continued to do so until lavage could be done. Examination showed a temperature of 98.6° F.; pulse 100, regular, and of good volume; respirations 26, and regular.

There was nothing abnormal in the child's appearance, and it showed no evidences of suffering pain. There were no further symptoms for two hours, when the patient seemed to have pain in the abdomen, was drowsy, and complained of great thirst. The pulse rate increased to 150, and within an hour the child's face became flushed, the respirations were somewhat labored and irregular, and there were evidences of impaired hearing and some hallucinations of vision. The temperature was not increased, but there were slight twitchings of the hands and the muscles of the neck, and at this time delirium was first noticed. There was diarrhea and a

strong odor of oil of gaultheria in the stools.

At 3 r.m. the temperature was 99.4° F.; pulse 132, and of good volume; respiration regular, but somewhat labored. At 3.30 r.m., seven hours after the drug had been taken, the child had a general convulsion, in which the arms and legs were extended, eyes rotated upward, head thrown back, neck rigid, but there was no arching of the back. The pupils were equal and were moderately dilated. This tonic spasm lasted about half a minute and recurred at frequent intervals. The pulse was of fair volume, but was slightly irregular, and the respirations were deep, labored, and gradually decreased in rate to four or five per minute. These symptoms increased until, finally, the child died of respiratory failure at 6.30 r.m.,

ten hours after the ingestion of the poison. About three hours before death the child was catheterized, and salicyluric acid was found in the urine. An autopsy was not obtained.

In view of the frequent use of oil of wintergreen as a therapeutic agent and the comparative rarity of poisoning by this drug, it may be of interest to note that von Rottenbiller believes that the poisonous effects are due to impure preparations, the result of imperfect methods. He cites cases of poisoning by oleum ricini, due to ricin in impure preparations, and thinks poisoning by oleum gaultheriæ analogous to these.

Hare and Wood,<sup>2</sup> from experiments on dogs, concluded that oil of gaultheria acted as a respiratory and vasomotor stimulant. While this result is verified by the reports of some who have observed cases of poisoning in man, it will be seen that in the case reported above there was at no time any evidence of respiratory stimulation, the only effect observed being depression, which became so marked as to be the immediate cause of death.

Gallaher<sup>3</sup> reports the case of a boy who after taking half an ounce of oleum gaultheriæ had marked gastrointestinal symptoms and an inordinate appetite, but no nervous symptoms. He recovered in two weeks, under a treatment which consisted of bleeding, leeching, and cupping.

Hamilton<sup>4</sup> reports a case in which there was almost entire absence of gastrointestinal symptoms. In his case a young woman took half an ounce of oleum gaultheriæ after having swallowed an equal amount of oleum morrhuæ. She had hallucinations of hearing and vision, extreme stupor, rapid pulse and respirations, and left hemiparesis. She recovered.

Pinkham<sup>5</sup> reports a case which lends added interest to the subject in showing its medicolegal importance. A woman took one ounce of oleum gaultheriæ to produce abortion. She died in fifteen hours, after showing symptoms of gastrointestinal and nervous disturbance.

Jewett, Halderman, and Pillsbury report fatal cases following the ingestion of from three drachms in Halderman's to two ounces in Pillsbury's case. In the latter case an unusual symptom was erythema and an intense itching of the skin.

Abel<sup>9</sup> reports a case seen by Dr. Ott in which the symptoms resembled those seen in acute alcoholism. The patient was a child aged three years, who died eighteen hours after taking one-half pint of oil of birch.

Van Wagenen<sup>10</sup> saw two fatal cases, one in a boy, aged two years, who died twenty-four hours after taking one drachm.

Beck<sup>11</sup> mentions a fatal case, and also refers to the cases of six soldiers who were made ill after drinking a tea which contained, among other ingredients, some oil of wintergreen. They all recovered.

Potter<sup>12</sup> refers to a case which is probably the same one mentioned by Beck, but he gives no reference.

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## THE SIGNIFICANCE OF URINALYSIS IN PREGNANCY, WITH ESPECIAL REFERENCE TO ECLAMPSIA.

## By Robert N. Willson, M.D., of philadelphia.

Opinions are so various at the present time with regard to the significance of urinary conditions during pregnancy, and especially with regard to the presence or absence of glucose or albumin, that a few pertinent cases in the experience of the writer have led him to briefly discuss the following questions:

1. What are the customary findings of urinalysis during a (clin-

ically) normal pregnancy?

2. What variations from the normal may be noted, and what is their significance?

3. What dependence can be placed upon urinalysis as a warning

of impending eclampsia?

The first question is by no means the most easily answered of the three, if one bases his reply upon the statements gathered from the current discussion of the subject by those who do purely obstetrical work. There seems to be as much diversity of opinion as to whether albumin or glucose may be found in the urine of a strictly normal pregnancy as there is with regard to the origin of these substances. One author states that a trace of either albumin or glucose has no significance, while another assures the student that the appearance of either renders the prognosis grave for the mother and child.

It may be stated as a general working rule, none the less, that the urinary picture which is normal for the ordinary conditions of life is also indicative of normal conditions in pregnancy. Just how far this principle will maintain itself will be discussed at a later point.

Question 1 then narrows itself down to the subquery: Can there be variations from the ordinary normal urinary picture which will

still admit of a clinically normal labor?

The answer must be a prompt one in the affirmative. Not only do parturient women sometimes give normal birth to healthy children in spite of urinary conditions indicative of possible misfortune; but sometimes the urine in such cases appears of such a character chemically and under the microscope as to promise a rapid fatality if the labor be not at once terminated.

The specific gravity may be constantly depressed, the quantity of urine may be large or small, the excretion of urea may be diminished or increased; or there may be albumin, glucose, or both, present in large or in small quantities; and still the labor may be an easy one, and clinically normal for mother and child in every other respect.

A more frequent picture is that of a pregnancy during which (especially when the gravid womb is occupying considerable space in the abdominal cavity) a so-called trace of glucose or of serum albumin is detected by the ordinary tests. Still more frequent, and such a common occurrence as to cause no surprise when noted, is the presence of delicate quantities of serum albumin, detected only

by careful methods and confirmed by control tests.

In a series of nearly 1800 urinalyses, made by the writer during the past two years, a considerable number of the examinations were in the cases of women in the later stages of pregnancy. Of the entire number of specimens of urine obtained from parturient women, only a comparatively small percentage (22 per cent.) were entirely free from albumin and sugar, while in no case in which glucose was noted was albumin absent. In nearly 60 per cent, at least a trace of albumin could be detected. In many of the cases the albuminuria began to manifest itself about the fifth month. In some it was not present until the last days before delivery. In a few it became evident directly before the appearance of active labor pains, its presence being discovered at times only by accident, if the term may be fairly employed.

When glucose appeared in the urine of a subject known to have not previously shown glycosuria, the occurrence, as a rule, took place at some time between the beginning and end of the last month of pregnancy. Occasionally there was a trace of glucose present throughout the pregnancy, often disappearing completely after the birth of the child. In no case in which, in the absence of other indications of acute or permanent renal change, small quantities of either serum albumin or glucose (not evident previously) were found present during pregnancy did the urine fail to regain its normal

character shortly after the birth of the child except in the few cases in which fatal eclampsia supervened.

In the majority of cases the urea elimination was that of the normal woman under ordinary circumstances other than those of child-bearing. Its excretion varied with the individual, and especially in relation to the diet and exercise. Occasionally the quantity excreted appeared persistently high, and just as often exceedingly low; but with no evident bearing upon the otherwise normal outcome of the case.

When the microscopic sediment indicated positive renal change the beginning of this change almost invariably appeared to have antedated the pregnancy, and, as a rule, continued after the puerperium as a permanent condition. Exceptions were noted even to this rule, however, and the following case furnished rather a striking example of the kind:

Mrs. W. E. T., aged twenty-one years, was seen by the writer in her seventh month of pregnancy on March 19, 1901. Her father had died of trauma, and the condition of his kidneys was unknown. Her mother had chronic nephritis, and died from acute meningitis.

The patient had always been strong and well except for two attacks of pneumonia, followed on both occasions by a complete recovery. Since then she had always been active. Menscs regular; no leucorrhœa. She had been married one year, her last menstrual flow having occurred seven months before. No headaches or dizziness; no swelling of the face, feet, or hands. On physical examination she was found well nourished, her skin healthy, no jaundice or œdema. Chest absolutely negative; heart sounds all clear and regular; arteries soft. The abdomen was that of advanced pregnancy. On examination the gravid uterus was found to contain a living fetus in the L. O. A. position. The pelvic measurements were all ample and normal.

The urinalysis on March 21st resulted as follows: 1011, acid, pale straw in color, slightly turbid, sediment scanty, white, and flocculent; albumin none, sugar none; microscopically, full of squamous and cylindrical cells, no casts, few leukocytes, no mucus, no crystals.

A request was made during the following week that another specimen be sent, for the reasons that the specific gravity was so low and because there was doubt in the writer's mind as to the estimated time of the pregnancy.

On March 26th the *urinalysis* was 1013, acid, pale straw in color,

On March 26th the *urinalysis* was 1013, acid, pale straw in color, albumin a decided trace, sugar none; microscopically, much squamous and cylindrical epithelium, many leukocytes, no casts, much mucus, no crystals.

An examination the following day (March 27th) showed 1027, albumin none, sugar none, heavy phosphatic clouding with heat; microscopically, full of uric acid crystals; no casts, much squamous epithelium, few leukocytes, considerable mucus.

The patient felt at this time strong and well. Fetal movements distinct. During the next month the urine remained negative except for a very high specific gravity, a urea output of 2.8 to 3.6 gm. per 100 c.c., occasional showers of uric acid crystals in the freshly voided urine, and once a heavy sediment of calcium oxalate crystals. No albumin; no casts. On April 15th the patient's feet began to swell. Although requested, the urine was not obtained until ten days later, when the urinalysis showed 1030, albumin, 6.6 gm. per litre; sugar none; urea, 2.51 gm. per 100 c.c. Microscopically, full of small hyaline and hyalogranular casts, many leukocytes, no renal epithelium, no crystals.

On the following day the albumin still measured over 6 gm. per litre, and there were present many granular casts and much renal epithelium, although the patient had been in bed and on a liquid diet for two days. Periodical pains began to be evident during the early evening of this day, gradually increasing, and after a labor of twelve hours the head of the child was on the perineum, and was delivered naturally, with a slight laceration. The latter was repaired at once, and both mother and child advanced through a normal

puerperium and adolescence.

At no time in this case was there a suspicion of renal involvement up to the time of the single appearance of albumin in quantity, one month before term, and followed by its complete disappearance. Its reappearance at some time during the last ten days before the birth of the child; its presence in large quantities, and above all the indication by the microscopic sediment of serious renal change, all made labor a dangerous prospect and raised the question as to the best course to pursue. The event proved that sometimes Providence allows us to rush on in safety, when in a different mood we would counsel prompt artificial termination of the dangerous condition.

This will be recognized as a case in which every feature of the urinalysis indicated danger of the much-dreaded eclampsia, and as one which, none the less, passed on to a normal labor and delivery. The urine one month later was nearly free from albumin (faintest trace) and casts, but unfortunately the patient has moved away from

this vicinity and has disappeared from view.

It may be briefly stated that cases have been noted in which the urine has contained as much as 4 per cent. or 5 per cent. of glucose during pregnancy, and yet the woman has gone safely through to term and a successful delivery. The same must be said of such instances as of the case just cited, that the probabilities are all against a favorable outcome. We are, however, more intimately concerned with the subject of albuminuric eclampsia, and will pass over other considerations for the present. It will be sufficient to say that cases are constantly being noted in which albumin is present throughout the course of the pregnancy; others in which it appears

early or late in its course; and in one or both, or neither, there may be casts and renal epithelium in abundance; and still there may be no departure from the normal in the labor.

In concluding his comment on this question, and partly by way of discussing Question 2 (What variations from the normal may be noted, and what is their significance?), the writer would simply say that most cases of pregnancy present minute traces of serum albumin in the urine, and that these can be detected if sufficient care be devoted to the search. Probably these traces are the result of pressure by the gravid uterus and of the consequent congested state of the kidneys. Sometimes there seems to be actual renal disease, and the ultimate cause may never become evident. Such cases must be placed in the category with those other problems that are too deep for our understanding; and when they go on to normal labor we should be thankful for the occurrence and content to accept the gift of Providence. Too often the urinary indications of renal involvement are verified by the dreaded onset of eclampsia, and too often, also, in such cases the opportunity is afforded on the autopsytable to ascertain the extent of renal damage.

Much stress has been laid by some writers upon a diminution in the elimination of urea in certain cases of pregnancy, both as an indication of impaired renal activity and of the danger of eclampsia. Certain it is that in most pregnant women the specific gravity of the urine is high (1025 and upward), and the urea output correspondingly large; or, to state the sequence of affairs more accurately, the urea is excreted in abundant quantities, and the specific gravity is correspondingly high. The true significance of the variations in the elimination of urea must be estimated as in all other conditions -viz., when the kidneys are doing their proper share of work they will excrete a normal amount of urea; when hampered or diseased, their urea output is diminished and sometimes becomes exceedingly scanty. The doubtful claim that a decided fall in the amount of excreted urea is ever a dependable indication of oncoming eclampsia will be referred to again in connection with the cases cited under Question 3. The highest importance must always be attached to the presence of renal epithelium in quantity; also to tube casts, especially when in large numbers, and when of the granular, blood, or epithelial varieties. Normal urine always contains a few livaline casts, which may be found if looked for with care. No normal urine contains many of the latter, however, and normal kidneys are never responsible for casts of the granular or epithelial types. The microscopic sediment in the majority of instances furnishes our most accurate guide as to the condition of the renal apparatus, and its critical study should never be omitted from the nrinary examination.

It remains to recall the fact that sugar (glucose, lactose, etc.) may often appear in small quantities, and that when confined to such inconsiderable amounts it has little or no practical significance, at least in the light of our present knowledge. When glucose is present in pathological or in permanent form it is interesting to note that there is present also, with few exceptions, some indication of renal change. We have yet to discover the real cause of the appearance of glucose, even in diabetes, but we have learned clinically that diabetic glycosuria is usually accompanied by renal sclerosis, and that its urine contains a renal sediment; and we have learned that the association is such a close one as to be valuable clinically for diagnostic purposes. The rule holds equally well in the pregnant woman and the non-pregnant diabetic. The presence of glucose, as already stated, is in itself by no means a grave sign, and in small quantities unattended by signs of renal incompetency can usually be ignored as far as concerns the outcome of the pregnancy. When it represents a diabetic condition, however, it assumes a new importance, furnishing the picture of a subject of a cachexia undergoing the greatest strain imposed by nature upon woman's vitality. Pregnancy under such conditions becomes a dangerous and questionable duty, instead of woman's trying but precious privilege.

In conclusion, Question 3 (What dependence can be placed upon urinalysis as a warning against impending eclampsia?) raises again an all-important and much-mooted discussion. The writer has already cited a case in which the urinary condition indicated serious renal change, and yet in which labor was carried on with entire exemption from eclampsia. He remembers with vividness a second case in the hands of a prominent obstetrician in which the urine had always been found normal prior to the pregnancy. Unfortunately, the urinalysis was omitted during the course of the pregnancy owing to confidence in the integrity of the renal function; and this case died in eclamptic convulsions. A third case is still under the care of the writer, and is interesting in that it presents the picture of a urine absolutely normal on the evening prior to the beginning of labor, a total absence of a history of nephritis, and yet a series of convulsions beginning while the fetal head was on the pelvic floor and continuing into the post-partum stage after an instrumental delivery. The following presents merely an outline of the case:

Mrs. J. F. E., aged twenty-six years; family history negative. One child living and well; forceps delivery after a long but otherwise uneventful labor. Seen for the first time by the writer on March 14, 1903, at which time the patient considered herself six months pregnant. The abdomen was very large, but the patient stated that this was also true of the first pregnancy. The right leg was swollen, also the right labium, the veins of which and of the right vaginal wall were swollen and tortuous. This condition was greatly relieved in the recumbent posture, and was evidently due to pressure in the abdominal cavity. The vertex was distinctly felt on vaginal exam-

ination, approximately in the L. O. A. position. Pelvic measurements were all normal.

The urine at that time was examined and showed, A. M.: 1010; albumin, faint trace; sugar, none; urea, 1.22 gm. per 100 c.c.; microscopically, full of squamous cells, no renal sediment, few leukocytes, no crystals; P. M.: 1020, acid, etc.; albumin, faint trace; sugar, none; urea, 2.80 gm.; no renal sediment, full of squamous cells.

From this time until May 18th, inclusive, the urine was examined weekly. On the latter date both the morning and evening specimens were examined. At no time during this period could albumin or sugar be detected. No casts and no renal epithelium were present. The urea averaged 2 gm. per 100 c.c., and on the last examination before labor began was 2.18 gm. On May 19 the writer was called because of colicky pains over the abdomen. There was some headache, and it was learned that the bowel had not been emptied for two days. At this time the patient was supposed to be about one month from term, but the abdomen appeared so large that oncoming labor was suspected, and the vaginal examination showed the cervix already dilating. After a long, slow labor of twelve hours the vertex was on the perineum. Convulsions suddenly supervened, following the second of which forceps delivery was carried out with the assistance of Dr. W. A. N. Dorland, and without injury to mother or child. The placenta was at once delivered with the hand in the uterus. An hour later a third convulsion took place, followed by a fourth, fifth, and sixth. The urine drawn by catheter showed the following: 1012, acid, etc., strong odor of decomposition; albumin, 1 gm. per litre; sugar, none; urea, 1.18 gm. per 100 c.c.; considerable number of hyaline and hyalogranular casts; no blood; considerable renal epithelium.

The patient was bled, and then transfused into a vein with normal salt solution. She was then kept in a steam bath almost continuously for six hours, when the kidneys again began to take up their share of the work. Consciousness was not fully regained for thirty-six

hours, though no convulsions occurred after transfusion.

The urine rapidly cleared up, until at the present time it is perfectly normal, and the patient free from evident impairment of the renal functions, and with no recollection of the ordeal.

Dr. Dorland has informed the writer of a case of eclampsia, recently seen by him, in which the urine was examined immediately before labor, and found to be normal, but in which convulsions

appeared and death ensued before morning.

We have studied cases, therefore, which have presented urinary pictures of seemingly grave import, but in which labor has followed a normal course; and, on the other hand, cases of dangerously obstinate, and even fatal cclampsia occurring in spite of kidneys in which, up to the moment of labor, were supposedly healthy. As a result of our study we are confronted with the question: Can

BENEDICT: NEW METHOD OF GASTRIC PROTEOLYSIS. eclampsia be accurately foreseen and avoided by the careful attendectampsia be accurately foreseen and avoided by the careful attendant upon the case; and does albuminuria, or even a renal sediment, and does also marking the careful attendant or pharmanal and approximately according to the contract of the careful attendant or pharmanal and approximately according to the careful attendant. predict with any degree of accuracy parturient or puerperal eclamp-Predict With any degree of accuracy Parturient of Puciperal ecoampat the present time: is approached.

1. Careful urinalyses should be carried out in all cases of pregnancy at frequent intervals, and with increased frequency as term

2. The most dependable indications of impaired renal function of impaired renal function and of probable eclampsia have been shown by general experience to be the presence of decided quantities of serum albumin, the diminution of the eliminated urea, and the presence of a microscopic renal sediment (casts, renal epithelium, blood, etc.). The character of the latter, when accompanied by the well-known clinical signs of the nepliritis, always constitutes a working basis for an estimate of the probability of imminent danger.

3. Even if the urine appear perfectly normal the possibility of eclampsia must be considered, especially in young women. Eclampsia in cuch cases is of causal coverity with that of cases in which ecumpsia must be considered, especially in young women. Ecually with that of cases in which

the urine has given due warning of impaired renal functions. 4. When eclampsia supervenes upon labor in a subject with previously (apparently) healthy kidneys, the tendency subsequently ranal functions if the patient enrives is toward a return to normal renal functions if the patient survives. This circumstance would seem to indicate still more strongly that

the kidneys may actually have been normal up to the time of a temporary embarrassment and suspension of function. 5. Until the nature and ultimate cause of uramia and eclampsia if would appear that urinalysis. are more thoroughly understood, it would appear that urinalysis, of the though not an unerring guide, is our most valuable index of the kidneys and our most trustworthy source of infor-

Condition of the kidneys and our most variable much or the hidneys and our most trustworthy source of information as to danger from such forms of toxiemia. 6. The prognosis seems to be vastly improved if eclampsia be mhatal hy managing hlanding fallowed hy various transferior with combated by generous bleeding, followed by venous transfusion with normal salt solution. These measures reduce and dilute the poison with a condition of the circulation and reliave the condition of the circulation in the circulation, and relieve the cardiac distress. Free diaphoresis and purging are of course indicated.

# $^{A\ NEW\ METHOD\ OF\ GASTRIC\ PROTEOLYSIS.^{2}}$ $B_Y$ A. L. $B_{ENEDICT}$ , A.M., M.D.,

The essential chemical function of the stomach is the digestion of the stomach in the stomach is the digestion of the stomach in the stomach in the stomach is the stomach in the stomach is the digestion of the stomach in the stomach in the stomach is the stomach in th Proteids. While digestion of fats has recently been shown to take place in the stomach, as well as in the intestine, it is always insignifi-

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cant quantitatively. Digestion of (cooked) starches occurs within but not by the stomach, and may be very considerable, although no complete systematic study of this phase of digestion has been made as yet, and it is obvious that this phase of gastric digestion must be extremely variable. The method of gastric analysis submitted by the writer in 1900 to the Prize Committee of the American Medical Association, and published in the Journal of that body March 27-30, 1901, differed from the various clinical methods in vogue, in attempting to investigate directly the actual amount of digestive function performed, instead of measuring the acid, ferment or other potential energy remaining after the extraction of the stomach contents.

On account of the small quantity of raw material available in practical gastric analysis, the necessity of performing many manœuvres upon the clear filtrate, which seldom exceeds 50 per cent. of the total quantity extracted, and the necessity of using separate portions of the filtrate for other methods of examination, as those for acidity, peptic strength, and qualitative composition, it became evident to the writer, very early in his preliminary study of the problem, that exact scientific analysis of proteids was out of the question, even if it could be adapted to the use of the clinician. For this reason it was decided to employ the general method of centrifugal precipitation, and to throw out of solution the various proteids in successive groups corresponding to the degree of peptonization, and employing as precipitants substances which should produce fairly bulky precipitates, which should not precipitate non-proteid ingredients of chyme, nor result in confusing mutual reactions. By consulting the qualitative tables of proteid precipitants collated by Ewald, Gamgee, and others, some idea may be formed of the very considerable amount of preliminary study required, as, for one or other of the reasons mentioned, most of the reagents suggested were found inapplicable to the problem propounded.

Anyone who has used the centrifuge to any extent in clinical estimations of any kind, will assent to the statement that the only safe rule is to base a volumetric reading on the minimum obtained after several successive centrifugalizations at a considerable speed. Whether the hand, water, or electric centrifuge is employed, the maximum speed obtainable for tubes of considerable size, without great risk of breaking the glass and spoiling the result, is 2000 to 2500 revolutions per minute. The writer has obtained identical results with the hand and water instruments, and has always centrifugalized until the precipitate suffered no further diminution in volume. Usually three centrifugalizations of two minutes or more each have been used.

As originally reported, three precipitates were compared, dealing in all instances with an investigandum of 10 c.c. of clear filtrate from chyme, and using graduated tubes, which enabled the readings to be made directly in percentages of this amount. These precipitates were, successively: soluble albumin, precipitated by heat alone; syntonin and albumoses, precipitated by saturation with ammonium sulphate; peptones, purin bodies, amido-compounds, etc., precipitated by phosphomolybdic acid.

From an investigation of about twenty normal cases and over one

hundred abnormal ones the following data have been obtained:

Minimum. Average or normal. Maximum.

Albumin . . trace. 2-4 per ct. 7 per ct.

Albumose . . trace. ½-1 " 3 " (faint cloud always remained in suspension.)

Peptone . . 5 per ct. 20-30 " 47 "

With regard to the last line, it should be said that less than 15 per cent. is rarely found, except some hours after a meal, or unless evidence of low peptic and acid power is forthcoming. The maximum precipitate given includes albumoses, the highest precipitate found for peptone alone being 36 per cent., and, otherwise, the highest for peptone alone or albumose and peptone together—albumose never being sufficient to increase the precipitate materially—being 33 per cent.

The albumose precipitate being always scanty and inconclusive for practical purposes, I have for some time followed the suggestion of Dr. G. H. A. Clowes, and have simplified the procedure so as to precipitate soluble albumin by heat and then all further products by phosphomolybdic or phosphotungstic acid. On account of the sharp demarcation between these two precipitates, it is unnecessary to decant from the former, but the volume of the second precipitate may be read beginning at the top of the first. The weight of the second will, however, compress the first considerably, say from 2 per cent. to 1 per cent., or from 4 per cent. to 2 per cent. For comparative purposes, the first reading is taken without this compressive effect.

It is of interest to translate these readings by volume into percentages by weight. The volume of albumin represents about one-fifth as much by weight. The volume of "peptone" by the last or phosphotungstic acid represents about four times tained by tannin, in those instances in which the absence of starch—which is also precipitated by tannin and which may be present when the qualitative test for erythrodextrin masks it—allows a comparison to be made. The tannin precipitate, in turn, represents about the same exaggeration of the percentage by weight as in the case of albumin. Thus, the volumetric percentage of peptone represents an exaggeration of the weight percentage by about 20. However, these statements are not intended in an accurate quantitative sense, but merely to afford a general idea of the magnification, so to speak, obtained from this method. Like other clinical methods, it

<sup>&</sup>lt;sup>1</sup> In the original report this was called acid albumin or syntonin. Although after the ordinary test meal all soluble albumin has become so through the action of acid, it is not acid albumin in the technical sense until it becomes uncoagulable by heat.

is intended only for comparative use, and must not be interpreted in too literal a sense.

So far as I am able to learn, there are no conditions liable to be encountered in stomach contents, obtained in the usual way and examined with a fair degree of promptitude, which interfere with or notably diminish the precipitates mentioned. Obviously, if the albumin precipitate were allowed to stand for a long time in either an acid or alkaline medium, resolution would occur, but no notable diminution of bulk can occur during the test as ordinarily performed. Nor, on the other hand, is there any extraneous precipitate obtained by boiling the acid filtrate, which can add to the apparent bulk of albumin. It may be remarked here that the properly prepared filtrate is almost absolutely free from mucin.

The precipitate by phosphomolybdic or phosphotungstic acid certainly does not consist of pure peptone. It was formerly taught that gastric digestion ended with the formation of peptone, but we now know that amido-compounds—using the word in a rather loose chemical sense—are formed, as in pancreatic digestion. I have noticed that in comparing the "peptone" precipitate of the same filtrate, before and after standing at room temperature for a day or two, a considerable diminution in volume may occur, which is probably due to chemical change beyond the stage of peptones proper. If so, the volume of the "peptone" precipitate is probably not materially exaggerated by the progress of digestion beyond the

nutritive stage.

The lower proteids having been already removed, the "peptone" precipitate of filtered chyme may theoretically include peptones proper, amido-derivatives of proteids, amido-acids of bile, ammonium salts, alkaloids, and purin bodies. Any considerable admixture of bile spoils the sample for any kind of systematic analysis. Moreover, bile acids would be precipitated by HCl and excluded from the investigandum, unless there existed an absence of free HCl. Ammonium salts do not interfere materially, for even a 10 per cent.—practically a saturated-solution of ammonium sulphate yields less than 1 per cent. volumetric precipitate with phosphomolybdic acid, and an amount of ammonium demonstrable by the ordinary rough tests is almost never found in chyme. Alkaloids are, of course, never present in any appreciable quantity. In my report in 1900 the statement was made that phosphomolybdic acid did not precipitate with normal urine, although a blue color was produced. This statement is incorrect, as a small (usually 1 per cent. to 4 per cent.) but perfectly distinct precipitate is produced. The experiment was repeated several times, so that the discrepancy cannot be ascribed to a single exceptional urine, and the observation is so simple that the personal equation need not be considered. Doubtless, there was some imperfection in the reagent obtained for the control experiments with urine.

I have noticed a peculiar reaction with starch. Phosphomolybdic acid does not precipitate with a solution of HCl corresponding to the ordinary maximum in gastric juice, nor with a concentrated solution of starch. When, however, phosphomolybdic acid is added to a concentrated solution of starch, also containing hydrochloric acid in gastric strength, a precipitate up to 4 per cent. by volume may be obtained. This reaction well illustrates a possible fallacy in dealing with complex mixtures of organic and inorganic substances, for, aside from mutual reactions to produce insoluble substances, which form an important part of inorganic analysis, a genuine precipitation may drag down other substances in a mechanical way, or various changes of conditions may influence the solubility of certain substances. It is obvious that the method of analysis described follows the plan of successive precipitation and removal which characterizes the "wet method" of inorganic analysis. It is equally obvious that organic substances do not interact with the same definiteness as inorganic and that the conclusions drawn cannot be so absolute. Nitrogen estimations have naturally suggested themselves as a means of gastric analysis, and have been employed in different ways by various chemists. Unfortunately, the estimation of nitrogen does not afford a clue to its source from this or that proteid or proteidderivative, and the nitrogen percentage of albumin, albumose, and peptones in the generic sense is nearly the same, while, on the other hand, nearly or quite as great variations of nitrogen percentage may occur within each of these groups. It is theoretically possible to analyze quite accurately the various proteids of chyme. The process is, however, altogether too difficult for ordinary clinical use, and I am informed that it is impossible, even for an expert chemist, to make such an analysis with the small quantity of investigandum available —usually less than 20 c.c. of filtrate, after allowing for the ordinary acid titrations.

In order to determine how far the so-called peptone precipitate might be increased by the reaction with purin bodies, the following experiment was applied to a number of cases-about ten in all. The liquid above the strata of albumin by heat and remaining proteids, etc., by phosphomolybdic acid was decanted and the precipitates dissolved, so far as possible, by liquor potassæ. The remaining sediment was again centrifugalized and was found to amount to about 0.5 per cent. (taking the 10 c.c. as 100 per cent.) by volume of a beautiful, navy-blue pigment. I am informed by chemists that this is a reduction product of molybdenum, of unknown constitution. It is, however, probable that the potassium hydroxide redissolves other than the strictly proteid precipitates. Still, from the a priori probability that non-proteid precipitable substances are present in minute amount, from the experiments with urine and with starch and HCl, it seems a warrantable deduction that the so-called peptone precipitate is not exaggerated by more than 5 per cent. (taking 10 c.c. of

original filtrate as 100 per cent.), and this possible fallacy does not interfere materially with the practical value of the test.

Realizing, then, that we are employing a purely clinical and approximate method of comparing the proteolytic power of different stomachs or of the same stomach at different times, the question presents itself, What practical conclusions can be drawn from the results? In looking over my tables, it has not been possible to recognize a definite relation between the proteid precipitates and any other single object of the routine examination, such as acidity. This is by no means a condemnation of the method. If proteolysis were a mathematical function of some other measurable factor, it would not be necessary to attempt the former investigation at all.

A priori, it would seem that the albumose precipitate or this and the peptone precipitate should rise and fall with the amount of eombined hydrochloric acid, but I cannot discover any such direct relationship. However, in a series of notes on gastric analysis, published in American Medicine in 1902–1903, I have shown the fallacies of the sodium-tungstate test for combined acidity, and that by alizarin is probably not much better. Incineration methods are not adapted to clinical study, but it is possible that a really accurate estimation of combined hydrochloric acid would show a correspondence to the proteolytic tests.

When the albumin precipitate is high and the peptone precipitate low, poor digestion is suggested. One of the reasons for abandoning the separate precipitation of albumose was that the intermediate position of this precipitate and its small amount prevented any positive deduction. It often happens, however, that there is an abundant precipitate in both or all three steps in the process. This suggests that there has been a recent acceleration in the acidifying or early stages of digestion, and certainly does not seem to indicate an impairment of digestion. On the whole, the most definite information seems to depend upon the amount of the final precipitate, which should amount to 20 per cent. to 30 per cent. Generally speaking, there is a fair correspondence between what has been alluded to as the optimum precipitates and a fairly normal acidity and ferment test. For instance, we may compare two tests made on the same case under similar conditions:

Total acidity.	Free HCl.	Combined HCl.	Albumin.	Albumo≈e and peptone.	Rennet test.	
48	22	19	trace.	8 per ct	Weak.	
90	45	29	1 per ct.	26 "	Strong.	

When the investigandum is obtained late after a meal the digested proteids are low, usually about 10 per cent., whether the hydrochloric acidity is excessive or nil. Disturbances of the normal distribution of acidity in general seem to be inimical to digestion. While the alizarin test may not be reliable for the estimation of combined hydrochloric acidity, any great difference between the readings of acidity

by dimethylamidoazobenzol and alizarin indicates fermentation acidity, and if the sum of free hydrochloric and so-called combined hydrochloric acidity does not nearly equal the total, the peptonization is usually low. For instance:

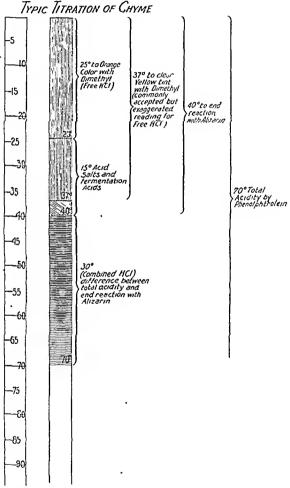
	Total.	Free HCl.	Combined HCl.	Fermentation.	Albumin.	Albumose.	Peptone.
F. G	85	15	27	85-(15+27)=43	1	trace.	10
J. B. B	. 78	S	53	17	4	34	22
G. L. S	. 77	10	. 50	17	. 5	trace.	31
M.	80	34	87	ð	2	*****	23
E. A. S	5. 78	28	33	7	traee.	*** ***	22
W. J. 1	3. 70	22	23	25	%	******	14
J. P.	89	* 41	25	23	4	3/4	17
c.	74	10	42	22	41/2	1	161/2

We cannot expect a very close correspondence in such examples, although I have selected several in which the total acidity is about equal. The phenolphthalein test for total acidity is fairly sharp and The alizarin reaction is sharp, but probably not very accurate. The dimethylamidoazobenzol test for free HCl is neither. As reported in the series of notes published in American Medicine, 1902-1903, the tedious method of titrating without an indicator and removing a drop of the investigandum from time to time and testing it with resorcin and sugar, has convinced me that an exaggerated reading for HCl is obtained, if we note the final but sharp end reaction with dimethyl. Instead, we must take the reading when the first slight but distinct change occurs from cherry to orange. This change occurs about fifteen degrees before the end reaction occurs, but I am unable to decide the point of change within an error of five degrees. As the alizarin method of estimating combined hydrochloric acidity is merely one of subtraction, it is immaterial for our present purposes whether this test is reliable or not, but the fact remains that when there is a considerable acid factor between the dimethyl reading and that by alizarin we may anticipate a low peptonization. This point may be illustrated by the diagram on opposite page. Unfortunately, we do not understand exactly how the acid salts and fermentation acids affect the various indicators. Apparently, a free organic acid acts precisely like a mineral acid, but much less energetically, and although I am convinced that the common practice of reading free hydrochloric acidity at the end reaction with dimethyl gives an exaggerated value and leads to the diagnosis of hyperchlorhydria in many instances in which there is really euchlorhydria—perhaps temporary—we must remember that all titration methods are purely approximate.

The method of proteolysis described, though approximately quantitative, must be thought of—like the acid estimations—as the measure of a rate of progress instead of a distance covered. There is no way of measuring the absolute amount of material digested by or in the stomach. We can, of course, weigh and analyze the entire test meal before ingestion and an hour or so afterward, resorting to thorough

lavage. But we cannot be sure that some portion of the meal has not passed the pylorus undigested; on the contrary, we can be reasonably certain that considerable loss has occurred in this way.

The method described is more simple and easy and, a priori, more logical than those based on measuring the "left-over" digestive power. That it is crude and contains fallacies, is obvious, but all methods applied clinically to the very meagre amount of investigandum obtainable are subject to this limitation. I am rather prejudent



diced in favor of the use of centrifugal volumetric estimations for various clinical purposes, believing them to be more accurate on the whole than gravimetric methods employed under the unfavorable conditions common to most clinical investigations and than most clinical adaptations of claborate methods, such as the Kjehlaahl nitrogen determinations. Meanwhile, assistance is desired in noting fallacies and in discovering more accurate means of separating the various proteids.

## THROMBOSIS OF THE MIDCEREBRAL ARTERY CAUSING APHASIA AND HEMIPLEGIA.

BY CHARLES W. BURR, M.D., PROFESSOR OF MENTAL DISEASES IN THE UNIVERSITY OF PENNSYLVANIA.

#### REMARKS ON CEREBRAL SKIAGRAPHY.

BY G. E. PFAHLER, M.D.

THE point to which we wish to direct attention in the following report is the usefulness of skingraphy in diagnosing cerebral disease and in locating the lesion. The importance of the method in tumor of the brain is well established. It probably will become of great value in the differential diagnosis of so-called uremic hemiplegia, in which there is no gross organic lesion, from hemorrhage and thrombosis. It may possibly prove to be an aid in differentiating between the two last conditions by means of the different location of the shadows, hemorrhage usually affecting the striate artery, thrombosis often of the main trunk as well as its branches. The patient's history is as follows:

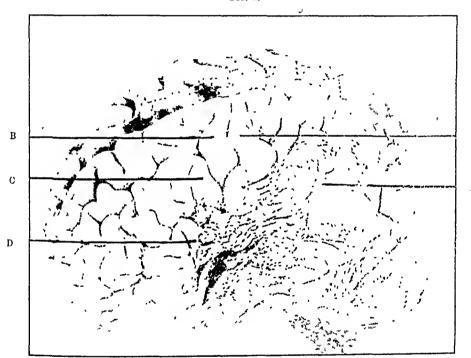
R. C., a white woman, aged sixty-seven years, was admitted to the Philadelphia Hospital in February, 1901. She had a rightsided hemiplegia and was aphasic. We learned but little of her previous history. Thirty years before her admission she suddenly lost power on the right side and became speechless. After several months sufficient power returned in the leg to enable her to walk a little, but speech never returned. Ever since the onset of the palsy epileptiform convulsions have recurred at long and irregular intervals.

When examined, the day after her admission, she could stand alone and, with the aid of a cane, walk a little. The gait was very hemiplegic. The right arm was completely and absolutely paralyzed. There was very slight palsy of the lower part of the face and none of the tongue. The right leg was slightly rigid. The right shoulder was very stiff, the forearm rigidly flexed upon the arm, but the wrist and fingers were relaxed. Passive movement of the right arm caused pain in the elbow and shoulder. The left knee-jerk was normal, the right increased. Ankle clonus and Babinski's reflex were present on the right side. There was slight wasting of the right arm from disuse, but no neurotic atrophy. Tactile sensibility could not be determined on account of the inability of speech. Sensibility to pain was certainly preserved. Her only speech was the recurrent atterance "no, no, no-no, no." This was expletive, not intellectual. It was spoken on every

<sup>1</sup> Read at the Pennsylvania State Medical Society, June 24, 1903.

attempt to speak, and I am sure that sometimes it was uttered unconsciously in direct consequence of some external stimulus without any willed effort. It probably, therefore, was, in the latter case, not even emotional, but purely reflex. She showed by gestures indicating their uses that she recognized the nature of familiar objects by sight, but of course she could not name them. She did not recognize written or printed words at all. She certainly recognized letters to be such and seemed to know the specific meaning of four or five. She recognized the nature and uses of familiar objects put in her left hand, but with the right hand she recognized

Fig. 1.



A. Dent in cyst wall. B. Ascending frontal convolution. C. Second frontal convolution.

D. Third frontal convolution.

nothing. The significance of this could not be determined owing to the impossibility of discovering the condition of tactile, weight, thermal, and space sensibility. It may have been caused by a disturbance of sensibility or been the result of a true cortical tactile amnesia. She could not write at all either from dictation or copy. She was not completely word deaf. She obeyed all simple verbal commands even when great care was taken that she should not be able to guess the meaning of the order from my gestures. Complex commands requiring long sentences to give she did not understand and did not obey. She could not understand any conversation except the simplest phrases. There was however, as I have said,

a remnant of word hearing left. She was not deaf to sound. While in the hospital she had several convulsions and several attacks of unconseiousness. She had chronie nephritis and died in a uræmie attack in April, 1902.

A necropsy was made the same day. Examination revealed extensive destruction in the region of distribution of the left midcerebral artery. The destroyed area was covered over by a pseudoeystic pial membrane. Fig. 1 gives a false impression in one regard, namely, the depression marked "A" is not, as it appears to be, a fissure surrounded by a convolution (the angular gyre), but merely a dent made in the cyst wall at the time the photograph was taken. The lower halves of the ascending frontal and ascending





Horizontal section of brain, showing atrophy of left side

parietal convolutions were completely destroyed; the upper halves were somewhat atrophied. Nothing remained of the island of Reil and only a small portion of Broea's convolution. The supramarginal, angular, and first temporal convolutions were absent. A part of the second temporal was also destroyed. The basal ganglia were quite a little smaller on the left than on the right, and the left internal capsule was atrophied. The anterior half of the posterior limb of the capsule was more affected than the posterior half. (Fig. 2.) The posterior horn and middle portion of the left ventricle were much enlarged and the outer wall was entirely lateral membranous, the cortex and underlying white matter being entirely destroyed. It is remarkable that the patient was not completely word deaf. The amount of speech hearing she possessed must have been due to the education and vicarious action of the right temporo-

sphenoidal lobe.

The case is interesting in many ways, for example, as regards aphasia and differences in vascular distribution, for it is probable that there is quite a variation in the arterial distribution in different brains, but I wish to use it here simply as showing the possibilities of skiagraphy in the hands of an expert such as my friend Dr. Pfahler.

Fig. 3.



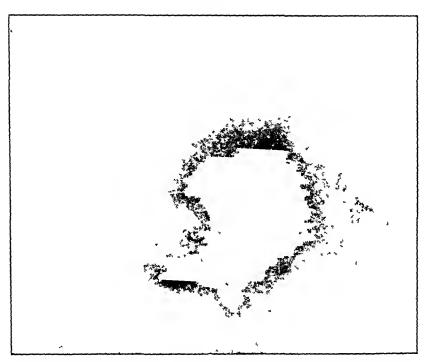
Skiagraph showing the outline of the skull, the frontal sinuses, the orbits, the base of the skull. The middle meningeal artery, the division between the cerebrum and the cerebellum, and the light area in the cerebrum corresponding exactly to the area of softening

Remarks on Cerebral Skiagraphy. By G. E. Pjahler, M.D.

At the February meeting of the College of Physicians of Philadelphia, I demonstrated, in connection with the case reported by Dr. Mills, that brain tumors can be skiagraphed. Some of these skiagraphs showed the absence of brain tissue, others a disturbance of brain tissue without any actual absence. Basing my opinion upon these facts I believed that an area of softening of the brain could be shown. My first opportunity to test this point developed at the autopsy in Dr. Burr's case just reported. The brain was replaced in the skull and an attempt made to photograph it by

means of the Roentgen rays. I first made a negative of the affected and then one of the opposite side, because I believed that possibly the normal side could be used for comparison with the diseased. The present case demonstrates, however, that this cannot be relied upon, for the lesion was shown upon both negatives, but with much more definite outline on that of the affected side. In studying a skiagraph it is important to recognize the shadows of normal structures first. If these are not shown well, abnormal shadows must be accepted with doubt. If, however, normal shadows are clear and definite, I believe that abnormal shadows will be of great value in making a diagnosis.

FIG. 4.



Skiagraph showing a normal brain in a skull prepared for experiment, also shows the outline of the skull, the two tables of the skull, the frontal sinus, which is unusually small, the sphenoidal and mastoid cells, and the external auditory meatus. The division between the eerebrum and the cerebellum may also be seen

In the skiagraph which I show of the affected side may be noticed the following normal structures: The outline of the skull, the orbits, the ethmoidal and sphenoidal cells, the sella turcica, the external auditory meatus, the groove of the middle meningeal artery, the division between the cerebrum and the cerebellum, and the peculiar striations which probably correspond to the convolutions of the cerebellum. Irregular shadows are also seen which are suggestive of the convolutions of the brain.

Above the cerebellum and petrous portion of the temporal bone may be seen the light area which corresponds to the outline of the area of degeneration. A light space is seen above the sella turcica which shows where the brain tissue had not been properly replaced. The saw cuts may also be seen. (Normal brain, Fig. 4.)

From an experience in fifty-five brain examinations I am convinced that the Roentgen rays will be of considerable value in the diagnosis of cerebral lesions. I believe that we shall be able to diagnose most large lesions, such as new-growths, softening, hemorrhage, and abscess.

# REPORT OF A CASE OF TUMOR OF THE BRAIN, AN ENDOTHELIOMA OF THE DURA; OPERATION; RECOVERY; DEATH IN 108 DAYS FROM RECURRENCE OF THE DISEASE.

#### BY WILLIAM J. TAYLOR, M.D.,

OF PHILADELPHIA,

ATTENDING SURGEON TO THE ORTHOPEDIC HOSPITAL AND INFIRMARY FOR NERVOUS DISEASES AND TO ST. AGNES' HOSPITAL; CONSULTING SURGEON TO THE WEST PHILADELPHIA HOSPITAL FOR WOMEN.

A BOY, aged fifteen years, born in America, of Russian-Jewish parentage, was seen first with Dr. Theodore Sprissler on January 25, 1903.

He had been perfectly well until ten weeks before, when he misbehaved at school, and his teacher, becoming angry, seized him by the neck and bumped the right side of his head against a wall. He came home and immediately complained of headache. Shortly after this, still complaining of headache, he was taken to see Dr. Theodore Sprissler, who examined his head carefully and could find no evidence whatever upon the scalp of any violence, as there was no abrasion, no bruise, nor swelling. He did, however, have some slight fever—a little over 100° F.—and Dr. Sprissler sent him home and to bed, fearing that he might be contracting typhoid fever, but he did not think that the knock on the head had anything to do with his condition. This fever soon passed away.

He did not see him again for some little time, and then only for headache, which the boy always complained of as being localized in his right temporal region. Of late this headache had become more marked and there had been some vomiting, but there were periods of entire freedom from pain.

Thinking the headache might be due to some ocular defect, he was sent to Dr. F. M. Perkins on January 20, 1903, who made this record:

"Examination. No external variation from normal appearances. Vision normal. Pupils respond to light, convergence, and accommodation. Neither eye goes out under covering hand; has full

vision with either eye and reads 0.5 type. Instilled homatropine

for ophthalmoscopic examination with following results:

"Right eye: media clear, H. 2 D.; veins and arteries slightly tortuous, but vessel contours nowhere blurred. No retinal or choroidal changes. L. E.: the same conditions exist as in right eye.

"January 21. Atropine sulphate 0.01 gives in either eye H. 2 D. Headaches still persist. Ophthalmic examination gives same ap-

pearances as on January 20th.

"27th. Patient was seen at office January 22d and 25th, and no changes in eye-ground appearances of January 20th noted, but on this date, at an examination made at the patient's home, the following was noted:

"Right eye: pressure neuritis; full, tortuous veins; lymph spaces full and at places contours of vessels almost lost; edges of disk hazy. Left eye: same conditions as in other eye, except in less degree."

The boy would have periods of headache, at other times was perfectly free from it, and during the time of freedom from pain ran around and played like other children, and attended school for five or six successive days before Dr. Perkins' first examination. These paroxysms of headaches were of such a character that at times he was thought to be shamming, but soon voniting occurred, and of a cerebral type.

In view of this condition, he suggested to Dr. Sprissler that I see

the boy.

Now there was a very slight swelling over the squamous portion of the temporal bone, about the point of the insertion of the temporal muscle, and this was the spot at which he complained of his intensest

pain, and it was somewhat tender on pressure.

When I saw him, on the 25th, the boy had been losing flesh, but there were no palsies. His station was perfectly good, but he complained of intense and increasing headaches, which were now almost constant, with occasional vomiting. I advised that he be seen by Dr. C. W. Burr, and also to increase the dose of potassium iodide, which he had been taking. The boy was evidently getting much worse, and on the 28th I saw him again, in consultation with Drs. Burr and Sprissler. We now were fully convinced that we had to do with a cerebral growth rapidly progressing. The symptoms had all increased; he had the most typical cerebral vomiting I have ever seen, and this occurred repeatedly while we were examining him. The slight enlargement on the right side of the skull had increased very materially and was extremely tender on pressure.

#### Medical Examination by Dr. Burr.

"I saw the boy for the first time on January 28th. On the right side of the head above the ear was a swelling about as large as a fiftycent piece and circular in outline. It was painful and sensitive on pressure. There was no palsy of either arm or leg, or of the face. He used the left arm a little awkwardly. Sensibility to touch was normal on the face, arms, and legs, and there was no astereognosis. The left knee-jerk was a little diminished; the right normal. There was no muscular rigidity, nor ankle clonus. Stroking the sole on either side caused quick and rapid extension of the toes. He could walk a little, but staggered much, and attempts at walking caused vomiting. I was not sure whether the staggering was due to ataxia or to weakness and the violent head pain. Several times during the examination he had attacks of cerebral vomiting. Speech was normal. His mental state was good. He did not like to talk much on account of the violent headache, but there was no clouding of consciousness nor was he mentally dull or silly. He answered all questions intelligently."

We believed the condition to be due to a growth of the skull, most likely an osteosarcoma, and that it was growing downward and producing pressure upon the brain, and not likely to be a growth of the

brain itself.

As he was growing so much worse and so rapidly, we all advised that he should be taken to St. Agnes' Hospital at once, and that his

skull be opened the next day.

On Thursday, January 29th, four days after he was first seen, I operated. His condition was growing rapidly worse; evidence of pressure had distinctly increased, the pulse was 56, the temperature was normal, and he complained of intense pain in his head. His head was shaved, washed, and the scalp thoroughly disinfected, and, in the presence of Drs. Burr, Perkins, Sprissler, and a number of others connected with the hospital, I made a large flap over the temporal region and turned down the scalp. The flap, which was oval, was three and one-half inches across at its widest point. found that a growth had eroded the skull and was attached to the temporal fascia and under portion of the scalp. This diseased portion I dissected away. I now with a chisel made a circular opening in the skull and lifted out a button of bone, two inches in diameter, the centre of which was the perforated portion of the skull. This was very vascular and evidently had undergone in almost its entire extent changes which, from macroscopic appearances, resembled sarcoma. In paring off the underlying growth I thought at first that I had opened into a large infiltrating growth of the brain. This was very dense and contained numerous fibrous bands. I next took a rongeur forceps and cut away the bone in front, at the back, and particularly toward the zygoma, and at last reached the limit of the growth: In working around the edges of the growth I found it was outside of the dura. The circumference of the dura was intact, but in the centre it had a base of about one inch, which was adherent. I now cut the dura completely around the growth and found a large tumor growing from the dura and projecting into the tissues of the

brain, but entirely free from attachments in every direction. This I shelled out without much hemorrhage. I used hot water to control the bleeding in the scalp and in the bone, as well as Horsley's putty, then packed lightly with iodoform gauze and closed the scalp.

He reacted well from the shock of operation and loss of blood, and in forty-eight hours the packing was removed. His condition was now most satisfactory: headache had ceased almost at once, his temperature had been good, but at the end of seventy-two hours there was evidence of a fungus cerebri. There had been comparatively little bleeding, but tremendous weeping of cerebro-spinal fluid, necessitating frequent dressing.

I did not believe at the time of operation that all of the diseased bone and dura had been removed, but all was taken away which had the appearance of disease. His condition was alarming, and I feared that he would die on the table from hemorrhage. I believed there

would be a speedy recurrence of the growth.

Every other case of dural tumor that I have seen, with one exception, has died from hemorrhage either at the time of operation or within the first twelve hours. The exception that I mention was a fibroma of the dura, removed by Dr. Keen in 1887. I have seen a number of other cases, and all have died from hemorrhage.

February 3d. Dr. Perkins made this note: "Ophthalmoscopic examination (in bed with candle-light) shows in each eye distinctly

made out contours of all vessels; no neuritis present."

By February 13th, or in fifteen days, he was up and about the ward. The wound had healed throughout, except at one small place, where there had been packing, and from this there still was a discharge of cerebrospinal fluid, but this was gradually diminishing each day, and ceased on the 15th. He had absolutely no pain nor tenderness, nor any interference with his eyesight, nor any evidence whatever of trouble with his brain.

February 21st. Dr. Perkins made this note: "Examination with student lamp at St. Agnes, boy sitting in chair in the dark room, conditions for examination thoroughly satisfactory. Right eye: no vessel tortuosities or dilatation; macular region is the seat of fine, silvery bands; otherwise fundus normal. Left eye: same ophthalmoscopic appearances as in other eye."

On March 6th, after an absolutely uninterrupted recovery, he returned to his home with the wound completely healed, except, possibly at one place, where there was a line of granulation about one-half inch long by one-eighth of an inch wide. The eye-grounds

were normal and he seemed to be perfectly well.

On March 12th he complained of a stiffness in the neck and inability to open the mouth wide, but this he had at the hospital, and was probably due to the irritation of the temporal muscles. He had no pain, headache, nor any symptoms of intracranial pressure, but there was certainly a greater amount of bulging at the site of the

wound than before. The whole of the flap was pushed out and there seemed to be a rather hard, nodular swelling beneath the scalp.

I believed the growth returning and sent him to Dr. Burr for his

examination and then to Dr. Perkins.

March 12th: Boy seen at his office by Dr. Perkins, who noted: "Pupils responsive to light, convergence, and accommodation. Neither eye out under cover; red Maddox rod, with rotary prism, with small electric light as object, gives at 20 cm.: exophoria, 0 to 2 degrees; hyperphoria, 0; and at six metres esophora, 1 degree; hyperphoria, 0. Right eye vision, 6/6; left eye, 6/6; no lenses used. Instilled homatropine for ophthalmoscopic examination, which gives the following findings: either eye media clear, and no pathological fundus appearances. The silvery macular bands noted on February 21st have entirely disappeared."

On March 16th, as there was distinct recurrence and no further operative measures could be undertaken, Dr. S. Mason McCollin began the use of the x-rays; but in two days there had been a rapid increase in the size of the growth, and he had slight headache, and his father noticed for the first time a slight discharge, which came from a small spot about one quarter of an inch in diameter at the upper anterior angle of the wound, and here and there at several spots over the surface of the projection were small points, which

evidently would break down in the course of a few days.

I had never seen such a rapidly progressing growth.

By March 22d he had grown so much worse and his weakness had increased to such an extent that he was no longer able to go back and forth to Dr. McCollin's office, and he therefore entered St. Agnes' Hospital for further treatment by the x-rays. The growth had enlarged very much, and his general condition was weaker; he was

pale, complained of pain in his head, and slept badly.

By March 31st the growth had increased somewhat in size, although this could only be estimated. He had had no headaches for a week, and this freedom must be attributed, I think, to the x-rays. He complained of a great deal of stiffness and pain in the neck, and of some numbness in the thumb and forefinger of the left hand, and stated that he could not move his thumb freely, although, when his attention was directed to it, it seemed to me that he could do so.

March 26th. Ophthalmoscopic examination made by Dr. Perkins showed in either eye slight vessel tortuosity, otherwise normal fundus. Red Maddox and rotary prism gave no muscle imbalance; and on April 2d: "In either eye the presence of undoubted neuritis, with swollen disks; the edges of the nerve entrance obscured, the vessel contour at places (even on general retinal level) being obscured for small areas. There was no evidence of enormous lymph extravasation or extensive hydraulic pressure, as was present at the commencement of the case—i.e., before operation—but the eye-

ground appearance was indicative of small encroachments on the calibres of the efferent vessels; presumably, therefore, commencing basilar interference. An examination made about four days before showed only vessel tortnosity, but no nerve head uplift above general retinal level. The Abney pellet test shows no central scotomata. There was no essential difference between the fundus appearances of either eye."

On April 13th he was taken to his home. He had now total paralysis of his left arm and hand, some paresis of his right hand; his speech was becoming impaired; he was very somnolent, sleeping almost all of the time, but he did not complain of much pain. Shortly after this he was placed under the care of another surgeon, who ligated the external carotid artery, evidently attempting to produce starvation of the growth by cutting off the blood supply. In this he was unsuccessful, as the boy died on May 17th, 10S days from the date of the removal of the tumor from the brain. No post-mortem examination was made by the physician then in attendance, and I did not learn of his death until some days after the funeral, and too late to make an attempt to procure one.

#### Remarks by Dr. Burr.

"I saw him again two days ofter operation. His condition was excellent. He was free from headache, bright and cheerful. There was neither anæsthesia nor palsy of either arm or leg. On March 12th he walked to my office and still was in excellent condition, except for a slight rhenmatic wryneck, which passed away in a few days. The tumor had, however, already begun to grow again, and I advised against operating a second time. When I first saw him the diagnosis of tumor of the brain was not difficult, but I was in error as to its nature. I thought it was most probably an osteosarcoma; it was an endothelioma.

"There is not the slightest doubt that Dr. Taylor's operation not only prolonged the boy's life, but gave him a period of entire relief from very serious symptoms. Had he not been operated on I am sure he would have died a few days after my first examination.

"The tumor, of course, affected only the prefrontal lobe. It pushed aside but did not penetrate the brain mass; it was not an infiltrating growth. Whatever relation there may be between the prefrontal lobes and mental processes, this case proves that there may be serious and rapidly increasing pressure on the right prefrontal lobe without any mental symptoms whatever."

#### Pathological Report by Dr. D. J. McCarthy.

"Sections were cut from the tumor mass, the dura, and the bone. Sections of the dura and its free edges showed the connective-tissue nuclei larger than normal, but there was no evidence of tumor-cell

infiltration. Sections of bone over the tumor showed a sclerated condition of the bone with absence of diploë, but there was no evidence of a malignant condition of the bone tissue. The sections from the tumor, and also sections cut through both the tumor and the dura, showed a tumor formation evidently starting from the meninges. The cells were arranged in rows following a racemose arrangement, and were in close contact with the interstitial tissue. Two types of cell were present: a large cell with small nucleus and relatively larger quantity of cell body, and a small round cell in the centre of the cell nests. The accumulations of cells in the dura between the bands of connective tissue gave somewhat the appearance of scirrhus, but the racemose type of infiltration following the lymph paths and the arrangement and type of cell lead us to make a diagnosis of endothelioma starting from the meninges."

### A REPORT OF FIVE CASES OF TUMOR OF THE BRAIN, WITH OPERATION.<sup>1</sup>

BY WILLIAM G. SPILLER, M.D.,

ASSOCIATE PROFESSOR OF NEUROLOGY AND PROFESSOR OF NEUROPATHOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

During my recent term of service at the University Hospital five cases of tumor, the growths being situated at different parts of the brain, were under my care, and in all operation was done by Dr. C. H. Frazier.

The first case was one of multiple sarcomatosis, and has been reported already in The American Journal of the Medical Sciences, July, 1903. A tumor was believed to be in the cerebellopontile angle, and it was found at this place. Multiple sarcomata of the central nervous system were not suspected before the operation, because they did not cause symptoms. I have already discussed this case and shown that symptoms of these numerous growths were absent because the tumors were so soft they caused no pressure and little or no destruction of tissue. This case is referred to here in connection with the other four, because all five cases occurred within a few months and in the same service.

Case II. Tumor of the motor area, correctly localized and operated upon, with much improvement in the patient's condition during a period of seven weeks; return of the growth, with fatal termination.—G. K. was referred to me by Dr. B. Kohn, April 21, 1903, with the following notes:

The patient denied having contracted syphilis, but said he had had gonorrhea. He had used alcohol formerly to excess. He had had

<sup>&</sup>lt;sup>1</sup> Read before the College of Physicians of Philadelphia, December 2, 1903.

toe was not moved. When a board containing movable letters was shown to the patient he was able to pick out six or seven letters correctly on command, and he, therefore, was not letter-blind. He said he had had very little headache on the right side of the head and that his headache had been especially severe in the left frontal region.

Dr. de Schweinitz examined the eyes on this date, and reported that the condition in the left eye-ground could not be considered positively a beginning choked disk, but that it was suggestive, and

within six months choked disk might be pronounced.

The patient was agraphic.

A diagnosis of tumor of the lower left motor area was made. It was supposed to affect Broca's area by pressure, or to invade it slightly, inasmuch as the motor aphasia was incomplete. The operation was done May 2, 1903, and a tumor was found in the opening of the skull, and was removed. Microscopic examination showed it to be a small spindle-cell sarcoma.

On May 5th, three days after the operation, my notes were as follows: The man can reply to questions, but still has much motor aphasia, and more than he had before the operation. The paresis in the lower distribution of the right seventh nerve and in the right upper and lower limbs is nearly the same as before the operation. He has no word-deafness. His general health is good, and he is very cheerful. The patellar reflex on each side is a little below normal. Ankle clonus is not present on either side. Achilles-tendon reflex, is about normal on each side. Babinski's reflex is not present on either side, and the toes are distinctly flexed. The biceps tendon, triceps tendon, and wrist reflexes are much diminished on each side. Stereognostic perception in the right hand is much impaired; but this may be the result of motor weakness.

By the end of May the man was able to be out of bed, and walked about the ward without assistance. He improved steadily, the right hemiparesis almost disappeared, his speech improved, his headache ceased, his cheerfulness was very marked, and he seemed to be almost entirely well. On June 20th he had a severe convulsion, involving the whole right side of the body, and he became paralyzed on the right side, but he soon regained some power in the paralyzed limbs. About July 7th signs of right-sided pneumonia developed. By July 16th the right upper and lower limbs had become completely paralyzed and speech was much affected.

July 25th. He has great difficulty in swallowing, and is completely paralyzed in the right upper and lower limbs. He can say only a few words, and these indistinctly. The biceps and triceps tendon jerks on the right side area little prompter than normal. The patellar reflex is about normal on the left side, but a little diminished on the right side. Ankle clonus and Babinski's reflex are not present on either side. Stereognostic perception and sense of position cannot

be determined, because of the difficulty in getting the man to respond. Sensation for pain is present in all parts of the body. The face is very slightly affected on the right side, and the tongue is protruded straight.

The man's general condition did not permit a second operation. He died July 26th with signs of pneumonia; but as the lungs could not be examined at the necropsy, we were in doubt whether he had

pneumonia or a tumor of the lung.

A necropsy was obtained, but permission was given for removal of only the brain and spinal cord. A tumor was found in the posterior part of the left second frontal convolution, extending into the middle of the precentral convolution and the upper part of Broca's area. The growth was infiltrating and at no part sharply defined from the surrounding tissue. It was, as already said, a small spindle-cell sarcoma. A small tumor about the size of a pea was found also on the right sixth cervical anterior root.

This case was seen in consultation by Dr. Mills, and he was also

present at the operation.

CASE III. Subcortical tumor, outer edge of tumor 1.5 cm. below the surface of the brain and within the white matter. Correctly localized as regards the portion of the brain affected, but not found at the operation because of its deep situation within the substance of the brain.—T. S., a male, aged forty-seven years, was referred to me by Dr. L.

J. Burns, April 27, 1903.

The man said he had contracted syphilis twenty-eight years previous. He had had a chancre, followed by sore throat and alopecia. He was married and had eight children living. His wifesaid that most of them were unhealthy and were anæmic. The wife had had four miscarriages. The man had had constant general headache during many years, but had had what he called "painful headache," confined to the left side of his face and head, during the last five years. He had paralysis of the right internal rectus; but this, he said, had been present for eight years. Since February 22, 1903, he had had convulsions, confined to the left side of the face and left upper limb. The convulsions always began in the lower part of the face, with a drawing sensation; then the jaws became locked, and the spasm extended to the upper distribution of the left seventh nerve. After the spasm in the face had reached its height, twitching of the left thumb was observed, and sometimes the left hand was forcibly rotated inward at the wrist. The left lower limb was never implicated in the convulsion. He had not lost consciousness more than once. The attacks lasted about three minutes. He had had as many as three or five in one day. When the attacks occurred he was unable to speak. He had attacks in which the speech became thick and convulsions did not occur. The warning was always a creeping sensation in the left lower jaw. He did not have nausea, vomiting, or dizziness. He complained of general weakness, but there was no

objective weakness detectable except in the lower part of the left side of the face. The biceps tendon and triceps tendon and wrist reflexes of the upper limbs were about normal. The patellar reflex was almost normal on each side. The Achilles jerk was prompt on each side, but a little more so on the left side. Ankle clonus and the Babinski reflex were not obtained on either side. The stereognostic perception was good in each hand. He had complained of a sensation of itching for years. His speech had been getting thicker during the previous two weeks. He had no tenderness on percussion of the scalp.

An examination of the eyes by Dr. W. C. Posey, April 28, 1903,

gave the following results:

O. D. inward motion abolished beyond the median line. Downward motion extremely limited, even down and out. External motion fully preserved. Upward motion lost. O. D. does not react to light or in accommodation. O. S. does react to light, but slowly in accom-Disks somewhat gray in their deeper layers. Vision: O. D. 5/12??; O. S. 5/5??

The man was admitted to the University Hospital, and while there a convulsive attack was seen by Dr. Willetts. It began with a creeping sensation in the left lower jaw; this was followed by twitching of the left platysma and of the left angle of the mouth. The entire left side of the face was drawn up, and the spasm was tonic. Flexion of the left thumb also was observed.

The report of the ophthalmic examination by Dr. E. A. Shumway,

May 26, 1903, was as follows:

Ophthalmic diagnosis: Paralysis of third nerve O. D.; paresis of fourth nerve. Partial retention of motion of eyelid; gray degeneration of optic nerves; sheaths full.

Vision: R. E., 6/12??; L. E., 6/7.5? A. R. E. 2 D., p.p. 18 cm.;

A. L. E. 0.75, p.p. 22 cm.

Pupils: O. D. pupil dilates to 7 mm. No response of iris to light or in accommodation. O. S. pupils responds sluggishly to both light and accommodation. O. D. lid droops slightly; movement inward entirely abolished; secondary contracture of external rectus, so that eye can hardly be brought to median line. Downward and upward motion lost, except slight down and out (fourth). O. S. movement

Eyegrounds: Media transparent; nerves show decided fulness of

perivascular lymph sheaths; gray atrophy of nerve.

Dr. Harland reported that there was no involvement of the larynx, but the soft palate and pharyngeal constrictors (right side) seemed

partially paralyzed.

On June 5, 1903, another examination was made. The tongue was protruded straight, and showed no tremor and no atrophy. The nasolabial fold on the right side was more distinct than on the left side. When the mouth was opened the teeth were not shown as distinctly on the left side as on the right. The patient could not draw up the left corner of the mouth alone at all, but could draw up the right corner.

Resistance to passive movements in the left upper limb was possibly not so good as in the right. The grip of the left hand was weaker than that of the right, and the left thumb was especially weak. The biceps tendon, triceps tendon, and wrist reflexes were about normal in each upper limb.

Resistance to passive movements in the lower limbs was about equal on the two sides. The patellar reflex was prompt on each side and equal on the two sides. The Achilles jerks were present and normal. Flexion of the toes occurred on irritation of the sole of the foot.

The left thumb felt numb, and the sense of position in the left thumb was much impaired, and the thumb was distinctly weak in resisting passive movements. Tactile and pain sensations were impaired in the left upper limb, and stereognostic perception was affected in the left hand. He called a dollar fifty cents, a twenty-five-cent piece a nickel. No impairment of stereognostic perception was detected in the right hand. Sensation for touch, pain, and temperature was not so distinct in the lower part of the left side of the face as in the right side. He called a pinprick sometimes a touch. The sensation of the upper part of the left side of the face was normal. He felt a pinprick less on the left side of the tongue, left side of the mouth and nose, and complained of a numb sensation in the lower part of the left side of the face like that in the left thumb.

Gait and station were normal, even with eyes shut.

A note was made that until the last two or three weeks his convulsions had always commenced in the lower left side of the face, and from here had extended to the neck, forehead, and eyeballs. Within the past two or three weeks, in five or six attacks, the convulsions had commenced in the thumb of the left hand, and had not extended farther than the wrist.

While under my care he had received mercurial inunctions and iodide of potassium until gastric symptoms developed.

A diagnosis of tumor of the right lower parietal and motor areas was made, because of the impairment of sensation in the lower left side of the face and in the left upper limb, and because of the impairment of stereognostic perception and sense of position in the left hand. The left lower limb was so little affected that the lesion was not believed to be high in the cerebral hemisphere nor to implicate the motor fibres of the lower limb in their passage to the internal capsule. Because of the convulsive movements of the left side of the face and of the left hand the tumor was believed to be cortical. An operation was performed by Dr. Frazier June 5, 1903; but, although a large opening was made, no lesion sufficiently intense to explain the symptoms was found.

An examination made June 23d, eighteen days after the operation, showed that the left upper limb was almost completely paralyzed. He could raise the left hand a little from the trunk while in bed. The grasp of this hand was very feeble. He could flex the left forearm slightly on the arm. The left upper limb was very flaccid. The biceps tendon and triceps tendon reflexes on the left side were a little exaggerated. The left lower limb was moved voluntarily and freely. The lower distribution of the left facial nerve was completely paralyzed, but the upper distribution was only slightly affected. The intelligence was good. The right side of the body was not affected.

The man had convulsions after the operation, and one of these was witnessed by Dr. C. K. Mills and myself, but the dictated notes were lost. My recollection is that they were typically Jacksonian

in type and were on the left side.

Dr. de Schweinitz examined the eyes July 6th, and reported: O. D., oculomotor palsy; gray disk, with distention of the central lymph sheath, no neuritis. O. S., external muscles apparently normal; no neuritis.

He was examined on July 8th by Dr. Frazier and myself. The mental condition was bad. He did not recognize anyone. He did not reply intelligently to questions. The right pupil was much larger than the left. He had become emaciated since the operation. The left upper and lower limbs were completely paralyzed. When the left limbs were stuck with a pin they were not moved; but the movements of the right limbs when the left limbs were irritated showed that the pain sensation was preserved in the latter. The left side of the face was only partially paralyzed. We could not determine by sticking the face with a pin whether the upper distribution of the left seventh nerve was affected or not. The left limbs were flaccid. The patellar and Achilles tendon reflexes were diminished on each side equally, but were not lost. The biceps tendon and triceps tendon reflexes were also much impaired.

On July 9th Cheyne-Stokes breathing was observed, and the man

was unconscious. He died on the afternoon of July 9th.

We had hoped to have a second operation. I felt sure that a lesion must be present in the area previously exposed, but the man's general condition was such that we could not feel justified in attempting another operation, especially as a very careful examination of the brain had been made at the first examination.

At the necropsy a tumor was found beneath the cortex, its central portion being below the right middle motor area. Its outer border was 1.5 cm. below the surface of the brain. The lower portion of the tumor was softened. The growth extended downward only as far as the upper level of the caudate nucleus, and at no place did it extend to the cortex. A line drawn across the brain from the fissure of Rolando would pass directly through the centre of the tumor. In

transverse direction the tumor measured 4 cm., and from before backward 5 cm. Microscopic examination showed it to be a mixed sarcoma, consisting of round and small spindle cells.

CASE IV. Multiple tuberculous tumors (méningite en plaque) of the parietal lobe, eorreetly localized and exposed at operation; removal of growths impossible.—F. F. was referred to me May 26, 1903, by Dr. Theodore B. Appel, of Lancaster, Pa., with the following notes:

The patient, a white man, aged thirty-one years, had been married some years, and had no children. The family history was obscure. The mother was alive and well. F. was splendidly developed physically, and had never been sick before the summer of 1898, when he was taken ill in Florida while serving as a volunteer, and was sent North. He was confined for six weeks in a Philadelphia hospital with typhoid fever and malaria. He recovered completely, and became a barkeeper in Lancaster. He acquired the reputation of being able to drink more and mix his drinks more than any man of his age. About July 1, 1902, he was taken ill with what his physician diagnosed as typhoid fever. He had a low fever for twelve weeks, never reaching 101° F., not accompanied by headache, intestinal disturbance, nor a great amount of depression. He was never the same man after this attack, though he went back to his work and returned to his habits as regards alcohol. He had been free sexually, but denied having contracted any venereal disease. After working for four weeks he was confined to his bed for five days with an attack of influenza. This was followed by recurrent headaches, becoming more and more severe, and both frontal and occipital. These headaches occurred every two or three days and lasted about twelve hours. The day following he usually felt well. About December 1st, while asleep, he had a rather severe left-sided convulsion, lasting about ten minutes. He came out of it somewhat dazed, but after a few minutes dressed and went to work. The next evening he had another convulsion, involving the entire left side, and after this he remained in a stupor about three hours. These convulsions, as well as all he has had, came without warning. He was still able to attend to his work, and about January 3d, while coming out of a saloon, he slipped and fell, cutting his head over the external angle of the left eye. He was unconscious about two hours, and he may have had a third convulsion, as the next morning he had partial loss of power in the left arm. The following week he had a very severe convulsion of a similar character, lasting about half an hour, and followed by still more loss of power in the left arm. On March 2d he had a peculiar staring look and rather slow, monotonous speech. patellar reflexes were very much exaggerated and the tonicity of the muscles on the left side was increased. After walking a short distance he had a tendency to bend backward, and he would prop himself against a convenient pole or wall until he had rested. He had decided loss of motion in the arm, but he could use it better

than he had done a month previous. He showed no signs of

syphilis.

On March 25th he had a fourth severe convulsion, limited to the left side, and followed by loss of power in the leg and left side of the face. Examination showed chronic inflammation of the optic nerves—more on the left side. He had some paralysis in the left side of the palate and throat muscles. He then was confined to bed. About April 10th he had another convulsion, which left him with the left side of his thorax absolutely paralyzed and an increased spasticity of arm and leg. His mental powers had steadily deteriorated, and occasionally he had visual hallucinations, and usually was like a child. His appetite was excessive. He had not had vomiting or fever. Occasionally he had involuntary evacuations of the bladder and he complained frequently of cramp-like pains in the spastic muscles of the leg and arm. The movement of the left thorax was very limited. Sensation for touch and pain was normal. The muscles of the left hand were slightly atrophied.

While under the charge of Dr. Appel he was treated with iodide

and mercury until he developed coryza, sore throat, etc.

I first saw F. F. June 6, 1903. He had then just arrived from Lancaster. He had a staring expression, suggestive of brain tumor; his intellect was much clouded, but he understood simple questions, and replied to them correctly. 3+2 he said = 6. 8-2=6; 8-4=4. His speech was thick and somewhat difficult to understand. His breath was offensive. He could move his head freely from side to side. The masseter muscle contracted firmly on each side. It was difficult to get him to draw up either corner of the mouth, and it was difficult to say whether or not the muscles about the corner of the mouth were weak, as he would not separate his lips. The tongue was protruded straight; it was not atrophied and showed no fibrillary tremor. The movements of the eyeballs were normal. Hearing was not determined, on account of the patient's stupor. He did not appear to be word-deaf.

The grasp of the left hand was fair, but not normal, and a little better than that of the right hand. Resistance to passive movement in both upper limbs was fair, but not normal. The muscles on the extensor surface of each forearm were somewhat atrophied. The biceps and triceps tendon reflexes and wrist reflexes were a little exaggerated on each side, but distinctly more so on the right side than on the left. His answers regarding sensation were not reliable, and yet when the upper limbs were stuck with a pin he made an effort to move them. The left upper limb was somewhat spastic; the

right was not.

The left side of the thorax was flat and moved very little in respiration. Dulness on percussion was obtained over the upper part of the left thorax. A cardiac pulsation and thrill were felt in the left second intercostal space. A murmur also was heard at this place, and was presystolic in time. Pulse was rapid, 112, and

regular.

The movements of the lower limbs were very weak; those of the left lower limb more so than those of the right. The lower limbs appeared to be weaker than the upper. He could draw up the right lower limb with difficulty, but could not draw up the left at all, and merely raised this limb from the bed. He was able to put both upper limbs above his head. The lower limbs were emaciated, and the left was very spastic and distinctly more so than the left upper limb. The right lower limb was a little spastic, but not nearly so much so as the left. The patellar reflex was exaggerated on each side. The Achilles jerk was exaggerated on the left side. The Babinski reflex was not obtained on the left side; the big toe did not move at all, and the other toes were flexed. The Babinski reflex was obtained on the right side, and the big toe was moved slowly and distinctly upward. The man was unable to stand even with support, as his legs were flexed on the thighs and the thighs on the abdomen. A bedsore was present over the sacrum.

I was informed by Dr. Appel that the man had lost power first in his left upper limb. Each convulsion began in the left upper limb; the eyes were turned to the left, and the face was contracted on the left side. The left lower limb was never involved in the spasm until

after the upper limb.

June 9th. Dr. Shumway reported as follows: Beginning optic neuritis; more decided in the left eye, in which the nerve shows some swelling. Nerve edges are obscured. Moderate tortuosity of veins.

Stereognostic perception is lost in the left hand and is normal in the right hand. He is unable to recognize a knife, pencil, or key with the left hand, but does so easily with the right hand. Sense of position is also lost in the left hand, and is normal in the right hand. He is unable to place the first finger of the right hand on the end of the first finger of the left hand if the eyes are closed. Pinprick is felt in both hands and forearms.

The left lower limb, except the toes, is almost entirely paralyzed. Any movement of this limb causes pain in the knee, and the knee is swollen; this possibly may explain why the weakness is greater than it was a few days ago. The patient is able to say correctly and without hesitation whether the big toe of either side is bent up or down; therefore, the sense of position in these toes is preserved.

11th. The mental condition is much better; he replies promptly to questions and understands better what is said to him. He does not draw up either corner of the mouth very far, but he seems to draw up the left corner a little farther than the right. When he closes his eyelids he has a peculiar fluttering of the upper lids, so that he is unable to keep the hids closed. He hears a low-ticking watch in each ear at the distance of about four inches. The grasp of each hand is feeble and about equal in the two hands. The interossei muscles in

each hand are somewhat atrophied and about equally so. The biceps and triceps tendon reflexes and wrist reflexes appear to be a little prompter in the right upper limb than in the left. Sensation for touch is much impaired, but not lost in the entire left upper limb, including a part of the left shoulder. Sensation for pain is almost normal in these parts, and both forms of sensation are normal in the right upper limb. The left upper limb is still somewhat spastic as compared with the right. He complains of tenderness on percussion in a spot about four inches directly above the external auditory meatus (probably the right side was meant). It is impossible to detect any change in the note in auscultation percussion of the head.

The left lower limb is very weak-much weaker than the left upper limb—and is very spastic. The right lower limb is apparently normal. The patellar reflex is much exaggerated on each side. The Achilles reflex is prompt on each side. The Babinski reflex is present on the right side, but feeble, and is not present on the left side. The lower limbs are emaciated and equally so. Stereognostic perception in the feet is uncertain. Sensation for touch and pain seems to be about normal in the lower limbs and feet. Ankle clonus is not obtained on either side. The patient is unable to stand even with assistance.

14th. Dr. de Schweinitz reported as follows: Double optic neuritis; 4 D.; right slight, and more extended in O. S. Paresis of right external rectus, with lateral diplopia in right field and nystagmic movement on right outer rotation. Visual fields normal with hand.

Convergence near-point poor. O. D. diverges first.

15th. When he is told to place the first finger of the right hand upon the first finger of the left hand with eyes closed he seems to have no idea of the position of the left hand, and can touch his fingers only by feeling his way along the hand. If the hand of the examiner be placed near the patient's left hand he may touch the former and think it is his own hand. His mental condition has greatly improved. He has no hemianopsia. The left lower limb he can move with more power than he could a few days ago.

19th. The weakness of the left upper limb is greater to-day than it has been for several days, and the mental condition is not so good.

22d. The grasp of the left hand is more feeble than it has been since the first few days after he came to the hospital. The movements of the left fingers are awkward. The left lower and upper limbs are spastic. The right upper limb is a little spastic. The biceps and triceps tendon reflexes and wrist reflexes are exaggerated on both sides. Diarrhœa is severe to-day. Mercury and iodide are discontinued.

Because of the greater weakness in the left lower limb as compared with the left upper limb, the loss of stereognostic perception and of the sense of position in the left hand, the impairment of tactile sensation with preservation of pain sensation in the left upper limb, the ataxia of the left hand, and the convulsive movements of the left side, a diagnosis of tumor of the right parietal lobe, encroaching especially upon the centre for the lower limb, was made. An operation was done by Dr. Frazier on July 23, 1903, and numerous small plaques were found in the right parietal region, extending into the area for the lower limb. They were too numerous to permit of removal

An examination made July 25th, two days after the operation, showed that the man's mental condition was poor. He did not move his left upper limb when asked to do so. The left side of the face and the left upper and lower limbs were paralyzed, but he could move the left lower limb a little. He was said to move the right

limbs freely. The right lower limb was rigid.

He died a few days after the operation, and the necropsy showed that these plaques were almost confined to the parietal lobe, but extended onto the median side of the lobe and the upper part of the postcentral and precentral convolutions. One or two small plaques were found elsewhere. None were found within the white matter of the brain, except where they had grown inward from the pia. They varied in size, but some were about a half-inch in one diameter and were flat against the brain. The microscope showed that they were tuberculous.

Case V. Tumor of the right cerebellar lobe at its union with the pons, correctly localized, and operation attempted but abandoned before the dura was opened, because of the patient's serious condition.-W. C. B. was referred to me July 3, 1903, by Dr. W. F. Randall, of Dushore, Pa. The patient was a man past middle life. About Christmas, 1902, he began to complain of dull headache, not severe, and not occurring daily. During the past month or six weeks the headache had been severe. It had been frontal or occipital, and sometimes general; it came at any time, and usually lasted only a short time. The patient began to vomit about April, 1903; at first he vomited only in the morning, but now vomits at any time. Dizziness does not appear to have been present. He has not had convulsions. His sight has been poor for two months; his intelligence is good. He has been growing weak during the past three weeks, and the weakness is general—not greater on one side than on the other. The grasp of the hand is good on each side. The movement of the lower part of the right side of the face is not so good as that of the left side. The forehead is moved voluntarily and equally well on each side. He closes the eyes firmly on each side. The tongue is protruded straight, and not atrophied. Voluntary movements of the upper limbs are free, and the grasp of each hand is good. The biceps tendon and triceps tendon jerks and wrist reflexes are about normal on each side. Touch and pain sensations are normal in the face and upper and lower limbs. The patellar reflex is prompt on the right side but diminished on the left side. Ankle clonus and

Babinski's reflex are not present on either side. He has dizziness when he sits up, and in walking staggers and always toward the right. He is unable to stand erect with feet together, and his wife says that his tendency to fall is always toward the right. His

memory has been failing during the past month.

July 16th. The patellar reflex is diminished on each side—a little more so on the left. Ankle closus and Babinski's reflex are not present on either side. Achilles jerk is present but diminished, and more so on the left side. Hemiasynergy is very pronounced in the right lower limb, and is not present in the left. When the right leg is flexed on the thigh and the thigh on the abdomen as far as possible, and then an attempt is made to extend the right lower limb, he extends first the right thigh, and later, when the limb is almost ready to be placed upon the bed, he extends the leg on the thigh.

The patient's wife said that before he came to the hospital he

yawned much in the daytime.

He has no tremor in movement of the upper limbs. He places the

first finger of either hand on the end of the nose well.

The report of the ophthalmic examination by Dr. de Schweinitz is as follows: Double optic neuritis (choked disks); swelling about 5 D.; many hemorrhages; paresis apparently of right external rectus; pupils prompt; right halves of visual fields contracted, but line does not run quite to fixation point left and only half-way right. They seem somewhat uncertain.

The report from Dr. B. A. Raudall is as follows: The right ear hears all tones less distinctly than the left, but distinguishes from 200-20,000 d. v. s. Bone-conduction preponderates over air, but is slightly subnormal where it should be exaggerated if trouble were tympanic only. Drumheads fair in appearance. No acoustic defect of left noted. There seems to be nerve lesion combined with tympanic on the right.

Examination of the blood showed: hæmoglobin, 75 per cent.; red

blood cells, 5,312,000; white blood cells, 9840.

23d. During the past three days the patient has had very severe attacks of headache, usually frontal, but occasionally occipital, and during these attacks he has been very restless. He has had some morning vomiting. His wife says that his mental condition is worse, and he does not understand what is said to him. Stereognostic perception is normal in each hand. Right hemiasynergy is distinct. Resistance to passive movements is normal in the upper and lower limbs. Some nystagmoid movement is present on looking to the right or left. Sense of position is normal in the hands, but the tests for the toes give uncertain results.

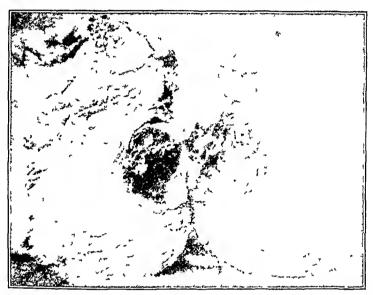
25th. The right side of the forehead is not wrinkled as well as the left, nor does he draw up the right corner of the mouth as well as the left. He yawns frequently. No tenderness of scalp is found on percussion. The patellar reflex is much diminished on the right side,

and not obtained on the left side. The patient has had fine twitching movements of the right extremities, although at times the movements have been on both sides of the body.

This case was seen by Dr. C. K. Mills in consultation.

An operation for the removal of a tumor believed to be in the right cerebello-pontile angle was done by Dr. Frazier July 23, 1903. The patient's condition was so serious that further operation had to be postponed after the bone was cut through. He died July 24th.

At necropsy a cyst was found in the right cerebellar lobe. Its inner wall extended to the union of the right cerebellar lobe with the pons. Its outer wall extended to the surface of the cerebellar lobe,



Photograph of the right lobe of the cerebellum from Case V The lobe has been cut in half The cyst, with a small tumor in its wall, is shown at the lower part of the cerebellar lobe. The upper part of the photograph represents the medulla oblongata

but not beyond. Small tumor masses were found in the upper and inner wall of the cyst, and these, under the microscope, had the structure of a spindle-cell sarcoma. The cyst, with the tumor masses in its walls, could be easily enucleated. It measured 3.3 cm. from without inward and 2.4 cm. from above downward.

The vessels of the brain had been torn away, and it was impossible to say whether thrombosis had occurred or not.

A brief summary of the last four cases is as follows:

Case II. The symptoms were paresis of the right side of the face and of the right upper and lower limbs, some motor aphasia, diminution of each patellar reflex, frontal and occipital headache, and convulsive movements of the right upper limb, but not of the lower. The patient did not have nausea, vomiting, vertigo, Babinski's sign, disturbance of sensation, loss of stereognostic perception, nor optic neuritis.

An infiltrating spindle-cell sarcoma was found in the second left frontal convolution, extending into the middle of the precentral and postcentral convolutions and the upper part of Broca's area.

Case III. Syphilitic infection was acknowledged. The symptoms were severe headache on the right side during five years, convulsive movements of the left side of the face and of the left upper limb, but not of the left lower limb, a little weakness of the left side of the face, and nowhere else, gray degeneration of the optic nerves, paralysis of one third nerve and paresis of one fourth nerve, and loss of the iritic response to light and in accommodation. The patient did not have nausea, vomiting, dizziness, optic neuritis, alteration of tendon reflexes, Babinski's sign, nor loss of stereognostic perception. Later, some weakness of the left upper limb was noticed, and sensation became impaired in the left upper limb and in the left side of the face, and stereognostic perception and sense of position became impaired in the left hand. Still later, the left upper and lower limbs became completely paralyzed, and motion in the left side of the face became imperfect. A subcortical mixed sarcoma (round and small spindle cells) was found in the right cerebral hemisphere. Its central portion was beneath the middle part of the motor area. Its outer border was 1.5 cm. below the surface of the brain.

Case IV. The symptoms were frontal and occipital headache, convulsive movements of the left side of the body, impaired mentality, some weakness of upper and lower limbs, greater on the left side than on the right, spasticity of the lower limbs, exaggeration of tendon reflexes, Babinski's sign on the right side, but not on the left; optic neuritis greater in the left eye, loss of stereognosis and of the sense of position in the left hand, impairment of tactile sensation, but not of pain sensation, in the left upper limb, and awkwardness of the movements of the left fingers. Numerous tuberculous plaques were found, almost confined to the right parietal lobe, except where they extended into the upper part of the postcentral and precentral convolutions.

Case V. The symptoms were occipital, frontal, or general headache, vomiting, general weakness, paresis of the lower part of the right side of the face, dizziness, staggering toward the right, diminished patellar reflexes, right hemiasynergy, frequent yawning, double optic neuritis, paresis of right external rectus, central deafness on the right side, some nystagmus on lateral movement, and impaired mentality. A cyst with small sarcomatous masses in its walls was found in the right cerebellar lobe at its union with the pons.

In Case II. the convulsions in the right side of the face and in the right upper limb, the weakness of the right side of the face and of the right upper and lower limbs, the partial motor aphasia, were indicative of a focal lesion, probably a tumor, in the left side of the brain, and chiefly in or near the centre for the upper limb. As the convulsions probably had not implicated the right lower limb, it

seemed more likely that the tumor had grown inward and involved the fibres coming from the centre for the lower limb in their course from this centre to the internal capsule. The absence of convulsions in the right lower limb seemed to indicate that the cortical centre for this limb was not irritated or else irritated after the fibres from this area had been cut. It was not surprising, therefore, to find a tumor within the brain in the area indicated. Especially noteworthy in this case was the absence of optic neuritis, nausea, vomiting, and dizziness.

The tumor was entirely removed, so far as we could determine, and was one of the smallest I have ever seen taken out at an operation. It was not very much larger than an English walnut. Our desire should always be to remove a tumor while it is still very small, but we are usually unable to accomplish this, as the symptoms are not sufficiently indicative of the position of the new-growth in its early development.

We felt very much pleased on account of the great improvement and, indeed, almost complete recovery following the operation for a period of about seven weeks. If the tumor had been well defined from the surrounding tissue a return might not have occurred. The necropsy showed a tumor that could at no point be outlined from

the surrounding brain tissue.

We were very desirous of making another attempt to remove the growth, but the man's general condition was not such as to warrant

this on account of signs of pneumonia.

Restoration to health for a period of seven weeks is by no means to be despised, and if, at the operation, we had removed more of what seemed to be healthy cerebral tissue surrounding the tumor the recurrence might have been prevented or delayed much longer. In every case in which a tumor is infiltrating and has the appearance of a sarcoma I would recommend that surrounding brain tissue should be removed, even though it appears to the naked eye to be healthy, and even though paralysis is likely to be increased by this removal.

In Case III. syphilis was acknowledged, and the headache existing many years, the paralysis of the right internal rectus extending over a period of eight years, and the loss of the iritic response to light and in accommodation made the case appear as one of syphilitic meningitis. Antisyphilitic treatment was thoroughly employed, without distinct benefit, but this did not prove that the case was not one of syphilitic meningitis. I have seen vigorous administration of mercury and iodides have little effect on advanced cerebral syphilis where many symptoms suggested the existence of brain tumor. These cases should be regarded, at least clinically, as cases of brain tumor, and so treated—i.e., by operation, where operation is permissible.

The convulsions involving the left side of the face and the left

upper limb were indicative of a lesion in the corresponding cortical centres for these parts. At first there was weakness only in the lower part of the left side of the face, but later the left hand-grasp became weak. The stereognostic perception became impaired in the left hand, the sense of position became impaired in the left thumb, and tactile and pain sensations became impaired in the left upper limb. Sensations of touch, pain, and temperature also became a little impaired in the left side of the face. The lesion seemed to be in the face and upper limb centres and the adjoining part of the parietal lobe, and it was believed to be cortical or very near the cortex, because of the typical Jacksonian epilepsy.

The area mentioned was exposed, but a distinct tumor could not be found. I regret that the brain was not punctured more freely in the exposed area. I have seen punctures made so often at operations for brain tumors without any effect, except possibly some increase in the paralysis after the operation, that I had grown a little lukewarm toward this procedure. In Case III, the tumor was softened and partly fluid in its lower portion, and repeated punctures might have caused the escape of some of the fluid and the detection of the tumor. It was so far below the cortex that its complete removal might have been uncertain, and, probably, would have been

impossible.

In this case, as well as in Case II., optic neuritis did not exist, and this sign was, therefore, absent in two of the five cases, and yet in each of the two cases the diagnosis of tumor of the brain was made. One was a tumor of the middle motor area, and the other a subcortical tumor of the lower parietal and lower motor area. Choked disk is one of the most common signs of brain tumor, but is not always present. Oppenheim, in his monograph on brain tumors, in regard to this subject says that he has found typical choked disk in fourteen and optic neuritis in five of twenty-three cases—i. c., in 82 per cent.; that Gowers found it in four-fifths of his cases, and Knapp in two-thirds of his cases. Oppenheim expresses the opinion that, as in recent years the diagnosis of brain tumor has been made earlier and confirmed by operation, choked disk is not so frequently seen. Although papillitis does not depend entirely on the location of the tumor, he thinks it is almost a constant and early sign of tumor of the cerebellum. It is relatively often absent when the tumor grows from the meninges and presses against the brain, also in cases of cortical tumors that do not penetrate far into the white matter, and of tumors of the pons, medulla oblongata, and corpus callosum. Tumors of the occipital lobe, he thinks, cause optic neu-

Mills,<sup>2</sup> in his text-book, remarks that optic neuritis is probably present on both sides in from 60 to 80 per cent. of all the cases of

<sup>&</sup>lt;sup>1</sup> Die Geschwulste des Gehirns, second edition, p. 63.

<sup>&</sup>lt;sup>2</sup> The Nervous System and Its Diseases, p. 510.

brain tumor, but that statistics on the subject are somewhat conflicting. It has been noted, he says, in only about 50 per cent. in tumors of the motor cortex.

Starr<sup>1</sup> says unhesitatingly that optic neuritis is present in 80 per cent. of the cases of brain tumor.

The occurrence of Jacksonian epilepsy in Case III., in which a tumor existed 1.5 cm. below the cortex, was somewhat misleading in making a diagnosis.

In the third edition of his text-book Oppenheim<sup>2</sup> says that unilateral convulsions may occur from lesions of the subcortical substance, especially when they implicate the fibres from the motor zone. The convulsions are not exactly like those of Jacksonian epilepsy, and when they resemble them more closely they are caused by lesions that affect the cortex by pressure, etc.

Dejerine,<sup>3</sup> in speaking on the same subject, remarks that typical attacks of Jacksonian epilepsy rarely may occur from limited subcortical lesions. He observed a case in which the convulsive movements began in the hand, and a tubercle was found in the white matter of the brain 1 cm. beneath the cortex.

In Case III. typical Jacksonian epilepsy was observed when the tumor was so far as 1.5 cm. below the cerebral cortex, and as the growth was 4 cm. in transverse diameter it must have been still further below the cortex when it first developed. This is possibly the first case in which a subcortical tumor so deeply situated caused typical Jacksonian epilepsy.

In Case IV. paralysis of the left side of the thorax was said to have occurred during a convulsion. The necropsy showed that the left lung was entirely at electatic. It seemed to me impossible that the left side of the thorax could be completely paralyzed as a result of a unilateral cerebral lesion. I have never observed such a condition, and I am not aware that others have. Muscles on the two sides of the body that contract synchronously are not paralyzed by a unilateral cerebral lesion.

Especially interesting in this case, and of great diagnostic value, were the loss of stereognostic perception and of the sense of position in the left hand, the awkward movement of the left fingers, and the impairment of sensation for touch, but not for pain, in the left upper limb. These signs were indicative of a lesion of the parietal lobe. Absence of hemianopsia made an implication of the sensory fibres in the internal capsule and, therefore, a lesion near the visual fibres, improbable, and the typical Jacksonian epilepsy pointed to a cortical lesion.

The loss of the sense of position was so marked in this case that the patient was unable to find his left hand with his right hand when

<sup>&</sup>lt;sup>1</sup> Organic Nervous Diseases, p. 600.

<sup>&</sup>lt;sup>2</sup> Lehrhuch der Nervenkrankheiten, third edition, p. 605.

<sup>&</sup>lt;sup>3</sup> Sémeiologie du Système Nerveux, p. 523.

his eyes were closed, and he frequently took hold of my hand believing it was his own.

Although I fully believe that a lesion of the parietal lobe may cause ataxia, loss of stereognostic perception, and loss of the sense of position and some disturbance of tactile and possibly of pain sensation in the limbs of the opposite side, I have not been convinced that a lesion of the motor area will give none of these symptoms.

In a recent paper Marinesco¹ remarks that Jonesco removed a part of the cortical centre for the left upper limb in a man. After the operation the patient could move his shoulder and elbow very well, but not his hand. Nine months later the movements of the left hand were very imperfect, and tactile sensation, the sense of position, and stereognostic perception were diminished in the left hand. In another case Jonesco removed the centres of the face and upper and lower limbs of the right cerebral cortex. A year after the operation there was much weakness of the left side of the body, and the sense of position, stereognostic perception, and tactile sensation were affected in the left upper limb. Thermal and painful sensations were preserved. These operations were done for epilepsy, and in one case, at least, and probably in both, the cortical motor areas were determined by the electric current.

I have observed loss of stereognostic perception caused by lesions much below the cortex of the brain, viz., in a case of tumor of the pons (Potts and Spiller) and in a case of tumor compressing the medulla oblongata (case of Dercum); but where the symptoms indicate a tumor of the cerebrum that probably is cortical, I believe the loss of stereognostic perception and of the sense of position and ataxia of the upper limb of the side opposite to that in which is the

lesion indicate much implication of the parietal lobe.

In 1898, at a meeting of the Philadelphia Neurological Society, I<sup>2</sup> referred to a case that I had seen in the service of Dr. Lloyd, at the Philadelphia Hospital, which seemed to show that the cortical representation of the sense of position is in the parietal lobe. A man complained, during the night preceding his attack, of fatigue, headache, and inability to sleep. The following morning he fell on the floor on attempting to rise from his bed, but was not unconscious. When he was found he had paresis of the left limbs and of the left side of the face and tongue. Later the patient could raise his left upper limb above his head, but every movement of this limb was ataxic in an extreme degree, though the limb was not paralyzed. The mental condition of the patient prevented an examination of the condition of sensation. At the necropsy a hemorrhage was found in the right parietal lobe. The hemorrhagic area was about 2 cm. in diameter, and extended inward in the form of a cone to the lateral ventricle, having its base in the cortex. It

<sup>&</sup>lt;sup>1</sup> Semaine médicale, October 7, 1983, p. 325.

<sup>&</sup>lt;sup>2</sup> Journal of Nervous and Mental Disease, January, 1899, p. 43.

was situated about 4 cm. from the longitudinal fissure and about 2 cm. or 3 cm. behind the Rolandic fissure. The brain had been cut into frontal sections about 1 cm. apart, when we had an opportunity to examine it, and, although the injury to the cerebral tissue prevented an exact determination of the location of the hemorrhage, it was evidently in or very close to the supramarginal gyrus. The ataxia was probably caused by a loss of the sense of position.

This was probably one of the first cases reported in this country, showing that ataxia from a loss of the sense of position may be caused by a lesion of the parietal lobe. The case of Starr and McCosh

preceded it.

A case that Dr. C. K. Mills and I saw together, June 3, 1901, in consultation, the case being under the charge of Dr. Ida Richardson, affords evidence also of the localization of the stereognostic perception and of the sense of position in the parietal lobe. The patient's left upper limb was decidedly ataxic, paretic, and astereognostic, and the head was retracted and rigid. The necropsy was made by Dr. W. F. Hendrickson. An area of depression, indefinite in outline, but about 6 cm. in diameter, was found in the parietal lobe of the right cerebral hemisphere just posterior to the fissure of Rolando. Palpation revealed less resistance at this point than over the surrounding tissue. On section this area was found to be the seat of extensive softening. The process implicated practically the entire right parietal lobe.

The case reported by C. K. Mills, which was seen by me and others in consultation, was one of the first to establish the localization of the stereognostic perception in the parietal lobe. A diagnosis of tumor of this lobe was made because of the loss of the sense of position, the impaired cutaneous sensibility, astereognosis, and ataxia. The case has been so fully reported by Dr. Mills and is so

well known that I need not refer to it further.

Oppenheim,<sup>2</sup> after giving a description of his case of parietal tumor with operation, remarks that lesions of the parietal lobe cause ataxia of one or both limbs of one side. Irritative or paralytic motor symptoms are absent, or when they occur they are the result of pressure. The sensory disturbance is always a partial hemian-aesthesia, in that pain and temperature sensations are preserved, while tactile sensation and especially the sense of position and the stereognostic perception are impaired or lost. Such a symptom-complex occurs when the lesion does not extend far into the white matter of the parietal lobe. He says, also, that the cases in which tumor of the parietal lobe has been so accurately diagnosed that a radical operation was possible are very few.

This case of Oppenheim was reported by him February 12, 1900,

<sup>&</sup>lt;sup>1</sup> Mills, Keen, and Spiller. Journal of Nervous and Mental Disease, May, 1900, p. 244.

<sup>&</sup>lt;sup>2</sup> Mitteilungen aus den Granzgebieten der Medizin und Chirurgie, 1900, vol. vi. pp. 382, 383.

and published in the third number of the sixth volume (1900) of the Mitteilungen.

In his monograph on tumors of the brain he says that in the majority of cases of tumor of the parietal lobe sensory irritative and paralytic phenomena were observed. He refers to Mills' case, but adds that the cases are not sufficient to permit us to regard the above-mentioned phenomena as positive evidence of lesions of the parietal lobe. The evidences of the localization value of these symptoms are, however, rapidly accumulating.

In March, 1901, C. W. Burr<sup>2</sup> reported a case in which there were slight hemiplegia, slight tactile anæsthesia, astereognosis, mind blindness, loss of the temperature sense on one side, sensory aphasia varying in intensity, and mental dulness. In this case a tumor was found in the parietal lobe, pressing against but not invading the ascending parietal convolution, partially destroying the angular gyrus, and involving almost the entire posterior parietal lobule.

The meningitis in plaques that occurred in Case IV. is of a very unusual character. The best paper on the subject that I know of is by Combe. He says that the meningitis in plaques (meningite en plaque of the French writers) is an unusual form of tuberculosis, and yet one that should be recognized. Tuberculosis of the central nervous system may appear as one or more tumors of different size, some small and some large; or it may appear as numerous minute tubercles scattered along the bloodvessels; or it may appear in plaques. Combe described the last form in 1898, although it was known to Landouzy, Dupré, and Chantemesse. The meningitis in plaques, as described by Combe, predominates on the convexity of the brain, and scarcely implicates the base at all. The inflammation is circumscribed and causes little exudation; it is almost always situated about and in front of the fissure of Rolando-i. c., in the motor zone. It occurs as one or several plaques of different size and thickness, and consisting of agglomerated granulations and fibrinous deposits. The pia is thickened about the plaques and contains miliary tubercles. The pia is normal over the rest of the brain, or else hyperæmic and thickened. The base of the brain, the interpeduncular space, the bulb, and the cranial nerves are not affected.

This form of meningitis does not cause basal symptoms; usually there is no vomiting, no constipation, no slowness and no irregularity of the pulse, no strabismus, no intense headache, no choked disk. The localization in the motor area explains the Jacksonian epilepsy and paralysis of the opposite side of the body. It is not surprising, therefore, that most of the cases mentioned by Chantemesse had not been correctly diagnosed from the clinical symptoms.

The common form of tuberculous meningitis occurs more fre-

<sup>1</sup> Oppenheim. Die Geschwulste des Gehirns, second edition, p. 116.

<sup>2</sup> The American Journal of the Medical Sciences, March, 1901, p. 306

quently in children, while the meningitis in plaques is found more

frequently in adults.

Combe<sup>1</sup> says that in every case in which the meningitis in plaques appeared to be primary, miliary tuberculosis or local tuberculosis not causing any symptoms has been found.

The dura is usually normal, but sometimes adherences with the plaques are found. The paracentral lobule is the part usually

affected.

According to F. Raymond<sup>2</sup> these plaques are really tubercles, and are caused by an infection conveyed by means of the cerebrospinal fluid.

E. F. Trevelyan<sup>3</sup> says that he has seen nine cases of the meningitis

in plaques.

In my Case IV. the plaques were situated behind the fissure of Rolando in the parietal lobe, and not in front of the fissure, where Combe says they are more commonly found. The dura was adherent to a few of these plaques. The optic chiasm examined by microscopic sections showed no evidence of meningitis, and yet

this part is usually a favorite location for meningitis.

In Case V. the movement of the lower part of the right side of the face was not so good as that of the left side. The patient always staggered toward the right in walking, and hemiasynergy of the right lower limb as described by Babinski was found on two or three occasions—i. e., when the right leg was fully flexed on the thigh, and the thigh fully flexed on the abdomen, and the patient then attempted to extend the limb and place it on the bed, the movements of the lower limb were not synergic; the leg was not extended simultaneously with the thigh. Babinski thinks that this hemiasynergy is present on the side on which the cerebellar tumor exists. I have observed the sign in four cases of supposed cerebellar tumor, but only in this, Case V., have I been able to establish its reliability by necropsy. In Case V. the patellar reflexes were diminished on each side. Deafness of central origin in the right ear was reported by Dr. B. A. Randall. Nystagmoid movements were present when the patient looked to either side. These were the chief signs that led me to diagnose a tumor of the right cerebellopontile angle, and the diagnosis was correct.

Repeated yawning was observed in Case V. I have seen this when the symptoms indicated a lesion somewhere at the base of the brain, and I look upon it as a sign of a lesion at this part and not in the cerebral cortex. Oppenheim thinks it is not a rare sign of cerebellar tumor, but I believe it may be seen in cases of tumor

elsewhere at the base.

I was unable to observe that the nystagmus was greater in devia-

<sup>&</sup>lt;sup>1</sup> Revue médicale de la suisse romande, 1898.

<sup>&</sup>lt;sup>2</sup> Leçons sur les maladies du système nerveux, 1900, fourth series, p. 24.

<sup>&</sup>lt;sup>3</sup> Lancet, November 7, 1903, p. 1276.

tion of the eyes to the right, the side of the lesion, than in deviation toward the left. In a case of cerebellar abscess that I saw in consultation with Dr. B. A. Randall the nystagmus was much greater when the eyes were turned toward the side of the lesion than when they were turned away from it. I have not been able to make this observation in any other case, but I speak of it in the hope that it may prove to be of clinical value.

Oppenheim describes involuntary movements, tremor; occurring in cases of cerebellar tumor, and such movements were present in

Case V.

## A DISCUSSION OF THE SURGERY OF TUMORS OF THE BRAIN, WITH A RESUME OF THE OPERATIVE RECORDS OF FOUR CRANIOTOMIES.

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THE statistics of the last five years give us every reason to take a more hopeful view of the surgery of cerebral tumors. It will be admitted without question that the greater attainments of more recent years are to be attributed to an earlier recognition of the tumor, to a correspondingly earlier resort to operation, to more accurate localization, and, finally, to certain distinct improvements in the technique. The latter may be said to include a speedier method of opening the skull, the exposure of a much larger area of the brain than was possible before the introduction of the osteoplastic flap, the adoption of the two-stage operation in those cases in which the blood pressure is materially depressed by the preliminary procedures. Many of the improvements or modifications of the technique in operations upon the brain have in view a common object, the prevention of shock. Operating as we are upon such a highly sensitive organ as the brain, and upon the organ which presides over functions so essential to the maintenance of life, additional precautions must be taken. precautions which one ordinarily takes to prevent shock in operations upon other organs must be observed in brain operations the more stringently; the avoidance of unnecessary exposure, the avoidance of unnecessarily prolonged operation, the prevention of excessive hemorrhage, the avoidance of unnecessarily rough manipulations of the tissue, the administration of the anæsthetic by an experienced man; careful observation of the patient's condition, more particularly of the circulatory function, throughout the operation at frequent intervals; these are all points to which the greatest importance should be attached.

METHOD OF MAKING THE OSTEOPLASTIC OR WAGNER FLAP. The instrument which in our experience at the University Hospital seems to meet every indication is the so-called dental engine armed with a trephine and drill. Given an area of brain to expose, an osteoplastic flap of corresponding size can be made with much less traumatism and in a much shorter time with this instrument than with any other. Objections to other instruments may readily be found. fashioning the flap with chisel and mallet a degree of traumatism must be inflicted upon the nervous structures within the skull, which is, to say the least, undesirable, and in the opinion of some surgeons the hammering increases the shock, and thereby adds to the risk of the operation. As compared with any of the other methods this is by all odds the crudest. The Gigli saw may be used, but a good deal of time is consumed in making the necessary number of trephine openings, and passage of the saw from one opening to another is neither an easy nor, in all cases, a safe procedure. The Stellwagen trephine, which was placed on the market a little over a year ago, is an ingenious instrument, but, from the mechanical point of view, is not to be compared with the dental engine. The efficacy of the Stellwagen trephine depends upon the ability to fix the central plate -this can only be accomplished by screwing the plate to the skull; but even after the central plate has been secured in place it requires a good deal of practice and force to be able to saw through the entire thickness of the skull in a reasonably short time. But there is still another and what I consider a very serious objection to this instrument, namely, the loss of a considerable amount of blood before the flap is reflected and the hemorrhage controllable. The greatest amount of bleeding comes from the venous channels in the diploë; with the Stellwagen trephine one begins to saw through the skull layer by layer from without inward until one reaches the diploë; upon reaching the inner table of the skull, one must proceed more slowly and with greater caution, because of the danger of penetrating the dura and injuring the brain. Meanwhile, hemorrhage from the diploic vessels is very free, and, of course, uncontrollable until the bone is entirely divided and the flap reflected. The drill of the dental engine divides the entire thickness of bone as it proceeds; furthermore, it seems to crush and occlude the openings of the diploic sinuses, and in that way spontaneously controls hemorrhage. Including the series of cases recorded in this paper, I have performed in the last six months some ten craniotomies with the dental engine, and I believe that with this instrument a given area of the brain can be exposed with the minimum degree of traumatism and in the minimum amount of time. The element of time plays a most important part in the outcome of operations for brain tumor. Mills,1 in a paper presented to the College of Physicians in 1902, said:

am satisfied that the present dangers to life in operations for brain tumor are from hemorrhage and prolonged operation." Therefore. the addition to our armamentarium of an instrument which economizes time will tend toward lowering the mortality. In the absence of complications it is quite possible without undue haste to completely divide and reflect the bony flap in eight minutes. It requires but very little practice to become proficient in the use of this instrument. After the incision has been made in the scalp, corresponding to the size and shape of the flap, an opening in the skull at one extremity of the incision is made with a small trephine operated by the engine. This will consume but a fraction of a minute. A small dural separator is inserted in the opening in order to make sure that the dura is free from the bone before the bone-drill is introduced. This can be attached to the engine without any risk of the operator's hand coming in contact with any portion of the engine that may not be sterile. The drill is now introduced and the bone divided from one extremity of the incision to the other. To guard against the possibility of the wound becoming infected from particles of dust that may be cast off from the arm or pulleys of the electric motor, an assistant plays a stream of sterile water or normal salt solution over the field of operation while the machine is in motion. But two objections to this method of performing craniotomies suggest themselves: onc, the possibility of infection; the other, the possibility of dividing the dura and lacerating the brain substance should the dura be adherent.

I have already referred to the manner in which infection may be guarded against. The danger of dividing the dura and lacerating the brain substance in those cases in which the dura is adherent is not incurred by this method more than by any other. No matter what the instrument selected for dividing the bone, if the dura be firmly adherent to the skull it will be exposed to the possibility of laceration. One of the advantages of making the flap of liberal dimensions is that there will be a margin of normal tissue between the lesion and the edges of the osseous opening. The possibility of the line of the bone-flap traversing the affected area is more remote.

McCosh, of New York, makes use of the electric engine in his craniotomies. A small bulb of the shape of a pear, about one-quarter of an inch in diameter, is attached to the engine, and with this bulb four or five holes are bored through the skull; the cone shape of the bulb allows the point to penetrate through the skull as it is revolved, and yet prevents the shaft from entering the skull or penetrating the dura. When the holes have been made the bulb is removed, and there is substituted a small circular saw, and the bone between the holes made by the burr sawed through. A small projecting and protecting flange is screwed to the side of the circular saw, so that the blade of the saw is exposed only for the depth of the skull as measured through the holes, and in this way the danger of sawing

through the dura is wholly obviated. This instrument would, it seems to me, require much more practice in order to enable one to operate it with safety. If one depends, in the adjustment of the flange, upon the depth of the skull measured at any one of the holes the danger of sawing through the dura cannot, as it is claimed, be wholly obviated. The depth or thickness of the skull varies, so that there would always be the possibility of the saw penetrating the dura if the skull were thicker at one of the holes than elsewhere, or what is also an objection, though not such a serious one, the saw would not penetrate the entire thickness of the skull if the skull were thinner at the point measured than it was at some other point along the projected incision.

Control of Hemorrhage. Exceptional precautions should be adopted to control hemorrhage from the very outstart. The amount of blood which will be lost from an extensive incision of the scalp might be considerable. The loss of blood will be reduced to a minimum by the application of a tourniquet around the head. have been in the habit of using for this purpose rubber tubing. Dr. Cushing showed me recently an appliance for this purpose which seemed to me very superior. It consists of an inflatable tube, which fits snugly the head of the patient, and with a small bicycle pump can be distended sufficiently to exert the necessary degree of pressure. If no tourniquet is used, it is a good plan to make the incision section by section, stopping to control the hemorrhage from one section before proceeding to the next. Hemorrhage from the diploic sinuses is satisfactorily controlled by Horsley's wax. When we come to the question of the control of hemorrhage from the brain and tumor itself, we are confronted with a more difficult problem. But two courses are open: one to pack gauze firmly into the wound, the other to close one or both carotids temporarily. The latter course would seem to be the ideal course were the practice of it unattended with risk. Crile, to whom we are indebted for this suggestion, performed this preliminary operation in a series of cases without any serious after-effects. It seemed to me that, if as in Crile's hands this operation were free from danger, a very important contribution had been made to the technique of brain surgery. My personal experience, however, has not confirmed these views. In the first place, temporary closure of the carotids does not altogether control hemorrhage; it controls arterial hemorrhage, but upon the venous hemorrhage, which is the much more troublesome, it has little effect. in addition to the control being ineffectual, it is not unattended by risk, at least it has not been in my hands. I have practised temporary closure of the carotid but five times in all, including two of the cases in this report, and from this limited experience I am firmly of the opinion that Crile's method should be reserved for the extreme cases, and in these should be confined to one side.

The posture of the patient during the operation should, of course,

<sup>&</sup>lt;sup>1</sup> Starr. Journal of Nervous and Mental Disease, July, 1903.

not be overlooked. Hemorrhage will be less free if the patient's head and body are well elevated. Unless the patient is in a state of shock I am in the habit of continuing elevation of the head and shoulders after the patient is transferred from the operating-table to his bed.

OBSERVATIONS UPON THE BLOOD PRESSURE. One of the signs of increased intracranial tension of whatever origin is elevation of the blood pressure. It is present in depressed fractures of the skull, in intracranial hemorrhage, in cerebral contusion and concussion, as well as in brain tumor. In a very exhaustive work on concussion and cerebral compression by Kocher and his students, the effects of intracranial tension upon the circulation of the brain were studied. It was observed that when the compression was of a very moderate degree there developed primarily a venous stasis or disdiamyrrhosis. This was due to the obstruction of the venous circulation by the increased intracranial pressure. If this pressure continues or increases the circulation of the brain becomes re-established; this phenomenon is attributed to a stimulation of the vasomotor centre, which, acting through the peripheral vessels, causes such an increase in the arterial pressure as will compensate for the increased cranial tension. And so it is that in the presence of a brain tumor we often find the blood pressure elevated above normal. In all operations for the removal of brain tumors I have made it a practice to make an observation of the blood pressure before the operation and to have the observations upon the blood pressure continued throughout the operation. These observations are recorded on a chart designed for this especial purpose; on it are recorded by an assistant a tracing of the pulse and blood pressure in such a way that the operator can see at a glance what the pulse rate and degree of blood pressure may be. The sphygmograph, which is used in my clinic, is very simple in its construction, and can be operated without any difficulty by an untrained assistant.

The object in having this record made throughout the operation is twofold. In the first place, generally speaking, the condition of the blood pressure is the most reliable index of the patient's condition; when the normal blood pressure is sustained throughout the operation we are assured that the operative procedures have not been of sufficient gravity to induce shock. This applies, of course, to operative procedures generally, and is not confined to those upon the brain; but in operations for the removal of tumors of the brain the blood pressure index is of much greater significance, in that it assists us in determining whether the operation should be performed in one or two stages.

Indications for Two-stage Operation. It has been said that 25 per cent. would be considered a conservative estimate of patients who died immediately from the effects of operation. In some cases death is attributed to shock, in some to concussion, and in some to

<sup>&#</sup>x27; It is a modification of the Riva-Rocci instrument that was worked out by Dr. Stanton, Instructor in Medicine at the University of Pennsylvania.

"unknown causes." In a discussion on the subject of brain tumors at the October meeting of the College of Physicians I said that I was inclined to believe that in the latter class of cases death was due to the sudden withdrawal of intracranial pressure. In the investigations of Kocher, that have already been referred to, it was demonstrated that the sudden withdrawal of intracranial pressure, after the blood pressure had been forced to a considerable height, may be followed by paralysis or break down of the vasomotor mechanism. If we are correct in assuming that this theory will explain many of the fatal terminations in a given number of cases, we should give more serious consideration to the advisability of dividing the operation into two stages. Horsley recommends the adoption of this procedure in every case without exception, and v. Bergmann, though not going so far as Horsley, recommended the two-stage operation in cases in which the patient's general condition was below par, or in which the tumor was a particularly large one. Horsley's recommendation seems to me unnecessarily radical, and that of v. Bergmann too indefinite. It seems to me a rule may be formulated which is based upon a much more scientific basis, namely, that when after the relief of pressure, such as would follow the removal of the osteoplastic flap and the reflection of the dura, there is a very decided fall in the blood pressure, an attempt should not be made at that sitting to remove the tumor. The completion of the operation should be postponed until the circulatory equilibrium has been restored, that is, until the circulation of the brain has become adjusted to the newly instituted physical conditions. This may mean the delay of a week or a delay of but forty-cight hours. [In order to determine in more exact terms the effect of the sudden removal from the brain of such pressure as would be exerted by a tumor, I am conducting a series of experiments upon dogs, in which an inflated rubber bag is introduced beneath the dura and distended so gradually as to simulate the growth of a tumor; when the bag is distended to a considerable size the fluid will be withdrawn suddenly, and the effect of the collapse of the bag upon the blood pressure will be recorded.]

In Case III. of this series such a course was adopted. The patient had a large subcortical tumor. Soon after the dural flap was reflected there was such a fall of blood pressure that I decided to postpone for the time being further operative intervention. The patient soon recovered from the effects of the preliminary step, but I feel quite sure that if I had continued with the operation and attempted to remove the tumor the circulatory disturbance would have been aggravated, and the patient would have died. In Case II. it will be noted in the chart that after the completion of the first stage of the operation the patient was not suffering from depression of the circulation. Accordingly, I proceeded and removed the tumor. The tumor proved to be a small one, so small that its presence had not caused enough increased tension to disturb the circulation, and the removal was effected, therefore, without affecting the blood pressure.

Sommer¹ reports his experience in an operation for sarcoma of the brain. Death ensued a few hours afterward for no demonstrable reason. The author says that in this as in many other cases death is due to sudden change in the circulation. His views coincide with mine. As a means of relieving pressure he recommends lumbar puncture in addition to the reflection of the osteoplastic flap as a preliminary measure, postponing for a few days any attempt to remove the growth. Lumbar puncture would no doubt relieve pressure temporarily, but whether its effects would be enduring enough to be of any practical value I am not prepared to say. Furthermore, lumbar puncture is in itself a dangerous procedure, and especially so in brain tumors. A number of sudden deaths have been reported as having been caused by this procedure.

As to the Question of Bulging of the Brain. If the most alarming feature of brain operation is hemorrhage, the most trouble-some is the bulging of the brain that follows reflection of the dura. In the course of our operations Dr. Spiller and I have made certain observations bearing upon this subject. As a preface to these observations it should be stated that a distinction is made between the bulging which occurs immediately after the dura is reflected, which will for convenience sake be termed "initial" bulging, and that which manifests itself during the subsequent exploratory manœuvres,

or "consecutive" bulging.

First, when a tumor is present there may be little or no initial bulging, but there is not likely to be any consecutive bulging. By this we mean that, given a case in which the tumor has been localized accurately and occupies the field bounded by the opening in the skull, there may be little or no bulging, even though the tumor be one of very considerable dimensions. In Cases II. and III. of this report there were present a small and a very large tumor respectively, and yet in neither case was there any initial or consecutive bulging. No doubt the character of the tumor would have some effect—thus a very vascular sarcoma would be more likely to bulge through the opening than a gumma. The release of pressure from a growth abounding in large vascular channels would result in a reactionary dilatation, more particularly of the venous channels, and this in turn might be followed by such circulatory disturbances as would readily lead to cerebral ædema. What we want to call particular attention to is this: that in the absence of bulging one must not be led to believe that there can be no tumor present.

Secondly, that when the tumor was not found, and if present was not situated at or beneath the area exposed, "consecutive" bulging was a very conspicuous feature, and the degree of bulging far exceeded the initial bulging observed when tumors were present. This at first thought seems as it were paradoxical, but upon further consideration is readily explained. It is due to the fact that normal brain tissue being the more sensitive reacts more rapidly to the insult of trauma-

Beiträge zur Psychiatrie klinik, 1902, vol. i. p. 5.

tism. When the looked-for lesion does not present itself on the surface of the brain at the site of exposure certain exploratory measures are instituted: the brain is palpated to determine its consistency, exploratory incisions are made into the cortex to determine whether the growth is subcortical, and the exploratory needle is introduced in the search for deep-seated collections of fluid. Meantime the brain surface is subjected to the injurious influence of a comparatively low temperature. Each one of these exploratory measures inflicts a traumatism of greater or less degree, and, as a result of their combined effects, the brain swells with amazing rapidity, so that within a few moments it protrudes so beyond the dura that it becomes a physical impossibility to replace it sufficiently to unite the edges of the dural wound. The actual cause of the swelling is no doubt the development of œdema. As pointed out by Cannon, who conducted a series of experiments in order to explain the secondary increase of intracranial pressure in head injuries, the swelling and pressure are wholly independent of any increase of blood pressure whatever, and are the result of certain chemical changes in the brain substance itself, whereby the osmotic pressure is so increased that the brain rapidly becomes cedematous.

The practical lessons to be learned from these observations are easily forescen. In the first place, have we not in this rapid and consecutive cedema a sign that the tissue presenting in the opening is chiefly normal brain tissue, and that if there be a tumor present in the region exposed it is in all likelihood a very small one? Secondly, these observations should teach us the importance of carrying out the exploratory measures in an expeditious manner. To be sure, we should not proceed with undue haste, but once the dura is exposed the various methods of exploration should be carried out in a methodical and unhesitating manner. A definite plan of procedure should be outlined before the operation begins, the instruments for exploration should be at hand, and once the dura is reflected the operator should, without a moment's delay, proceed with his investigation, and in the following order: 1. A careful inspection of the exposed cortex, noting whether pulsation is visible, whether the brain is of normal color, and noting the condition of the bloodvessels. Inspection should precede all the other forms of examination because soon after exposure of the brain to the traumatism inflicted by the examining finger the brain begins to bulge. The operator should palpate, gently of course, the cortex, both the part exposed and, if nothing abnormal be found there, the parts immediately surrounding. By palpation one can discover variations in consistency and in tension. V. Bergmann recommends in those cases in which the tumor cannot be felt that the patient be raised to a sitting posture, "whereupon the tumor may become visible or palpable, the area exposed sinking in somewhat from the atmospheric pressure in connection with the lessened blood pressure." 2. If by palpation one discovers an in-

<sup>1</sup> Woolsey. The American Journal of the Medical Sciences, December, 1903.

FRAZIER: SURGERY OF TUMORS OF THE BRAIN. crease in the consistency, and inspection fails to reveal a growth involving the cortex, an incision of from 1 to 3 cm. should be mid in the direction of the suspected lesion. The importance of making more than a nick in the surface of the brain needs no explanation In Case III., although the tumor would not have been removed at the first operation, it was not discovered, simply because the incision was not deep enough to expose it. 3. Failing to reveal the lesion an exploratory needle, constructed especially for this purpose, should be introduced in two or three directions, but always through the same opening. The instrument best adapted to this purpose is small cannula armed with a blunt obturator. The instrument should be introduced to the maximum depth, the obturator removed and the instrument gradually withdrawn. The ordinary exploratory needle is useless, because upon its introduction the orifice become plugged with cerebral tissue, and the communication between a cyst or an abscess is thereby cut off.

Given a case in which the brain has bulged to a very considerable degree, how should this complication be treated? Three courses are open to the operator: the first to attempt to restore the brain to its normal confines and to close the dural wound; the second to disregard absolutely the dura and to terminate the operation by closing the wound in the scalp; and the third, to make no attempt to replace the brain, but to repair the defect between the dural edges with a graft dissected from the pericranium. The adoption of one or the courses should depend upon existing condi-For purposes of illustration, imagine a case in which the tumor ha

not been found and in which there is an element of uncertainty in the diagnosis as to the existence of tumor. Under these conditions, if the dural edges cannot be approximated without such pressur upon the bulging brain as would lead inevitably to an undesirable amount of laceration of the brain substance, such a plan as that suggested by Keen should be carried out, namely, to dissect from the perieranium a graft large enough to fill the gap between the edges of the dura. This plan was adopted in Case IV of this series. A of the dura. This plan was another in Case IV. of this series diagnosis of tumor of the brain had been made, but instead of a manufactural property of the property of the brain had been made, but instead of a manufactural point of the property of the pro tumor a tubercular meningitis almost confined to the parietal lobe Was found. Shortly after the dura was reflected and the field explored the brain began to bulge in an amazingly and alarmingly rapid manner; to have attempted to suture the dura without removing a large section of the brain would liave been a physical impossibility, and inasmuch as there was no indication for the relief of pressure, th gap in the wound was closed in the manner as above described. A illustrating another phase of the question, Picture a case in which a tumor was undoubtedly present, but had been localized inaccurately a case in which headache was one of the conspicuous and most listressing symptoms. A radical operation in such a case is, for the me being at least, out of the question; but we have a case is not until

believe that in relieving pressure the patient will enjoy a temporary period of relief. If, then, the indication is clearly to relieve pressure, it would be the height of folly to attempt to sew up the dura, as by so doing the intracranial pressure would be as great as it was before the operation. Under these circumstances the dura should be disregarded absolutely, the bone of the flap should be removed, and the wound in the scalp closed with great precision.

PALLIATIVE OPERATION. In every operator's experience there will be a certain number of cases which for one reason or another are not suitable for the radical operation, either because the tumor is inaccessible, or because it may be too large, or because accurate localization is impossible. Under any of these circumstances when the patient is suffering, evidently from the effects of increased intracranial tension—e. g., headache, or choked disk—the palliative operation should be performed. I say "should be" because I believe an operation under these circumstances is more than a question of propriety; it should be regarded as imperative. Were it not for the headache the patient might enjoy for the rest of his days freedom from pain, if pressure is relieved. I have under my care now a patient that was referred to me by Dr. Hermance and Dr. Spiller, a patient who has unquestionably a tumor, but no symptoms sufficiently pronounced to make localization possible. He suffered from attacks of such violent headache that his reason became impaired; his suffering was intense and only to be compared with that attending the paroxysms of tic douloureux. Opiates did not relieve him. A section of bone was removed from the skull, and with but two exceptions, when the attacks were not severe and of very short duration, he has enjoyed absolute relief from pain, and is as contented and placid as one could be under the circumstances. The same gratifying effects may be obtained in cases of choked disk. When this condition has not existed so long as to have caused atrophy of the optic nerve an early operation for the relief of pressure will be followed by marked subsidence of or disappearance of the choked disk and by a corresponding improvement of vision. We are thus enabled to restore to a greater or less degree the patient's vision for the remainder of his life. In a case recently operated upon the effect of craniotomy and consequent relief of pressure was very strikingly illustrated. The choked disk, which was present to a very marked degree, subsided at least one-half within three weeks of the date of the operation. Unfortunately in this case the operation was not performed soon enough to save the patient's vision, as very marked atrophy of the optic nerve had already occurred. For the relief of these two conditions, namely, headache and impairment of vision, I lay stress upon the importance of the palliative operation. In performing this operation a section of bone representing about three square inches should be removed and a dural flap fashioned and reflected, and the wound in the scalp closed. This will afford the desired relief of tension.

RESULTS. As to the more recent statistics upon the results of surgical intervention for cerebral tumor, Woolsey has collected 101 cases of cerebral tumors which have been operated upon during the past five years. Of this series he says: "Twelve cases, 11.8 per cent., died within twenty-four hours, and twenty-six, or 25.7 per cent., within three weeks." Here at once we see a very marked reduction in the immediate mortality. Von Bergmann regards 25 per cent. as a very conservative estimate of the number dying as the direct result of the operation. Of the eighty-eight cases of Woolsey's series, of which an exact localization was made, the mortality was but 22.7 per cent., as against 46 per cent. among those not exactly localized. In Gussenbauer's series of twelve cases there was but one death, and that due to pneumonia. "As to the more remote results, six died within three weeks and three months; nine between three months and one year, and three between one year and two years. As almost all of these died from the effect of the tumor the mortality within two years is 43.5 per cent." This high mortality, both immediate and remote, Woolsey says is not greater than that following radical operations for malignant growths in some other situations, and that considering "the otherwise hopeless condition of these cases, the difficulties of exact diagnosis, the inaccessibility of the tumors, and the marked relief of symptoms in almost all cases not dying at once, we may take courage and feel some degree of satisfaction." Woolsey says "that we should feel still more encouraged when we consider the length of time during which some cases remain free of recurrences. Cases of sarcoma are reported four years, four years and one month, five and one-half years, and eleven years after operation. A case of fibroma was reported well eight years, cases of gummata two and one-half years, a case of glioma three and one-half years, and one case, in which the variety of tumor was not given, nine years after the operation. Seven cases of sarcomata are reported to have recurred at periods ranging from three months to eleven years, and averaging two years and four months, or, exclusive of the latter case, nine and one-third months."

It is needless to say that the prognosis in the case of benign tumors and cysts and in cases of well-encapsulated sarcomata is much better than in operations when the growths are of malignant and infiltrating

type.

RESUME. 1. All measures recognized as prophylactic of shock should be observed stringently. In these we have the most effectual means of reducing the mortality. The most important of them are (a) the avoidance of prolonged operation; (b) the prevention of excessive hemorrhage, and (c) the avoidance of unnecessarily rough manipulation of the brain substance.

2. A given area of brain can be exposed with the least minimum degree of traumatism and greatest economy of time by the electric

engine.

3. Temporary closure of the carotids in operations upon the brain is ineffectual and not unattended by danger. It should be reserved

for extreme cases, and practised on one side only.

4. Observations should be made upon the blood pressure immediately before and at frequent intervals during the operation. Object of same twofold: (a) as the most reliable index of patient's condition; (b) as the only exact method of determining whether operation should or should not be carried out in two stages.

5. Two-stage operation is indicated when there has been a decided fall in blood pressure after the relief from intracranial tension, such

as follows reflection of the Wagner flap and dura.

6. Lumbar puncture as a means of relieving pressure is a tem-

porary, not to say dangerous, procedure.

7. Bulging of the brain is one of the most embarrassing features of cerebral operations. A distinction may be made between that which occurs immediately after reflecting the dura, "initial" bulging, and that which follows as a result of subsequent exploratory manipulation, "consecutive" bulging.

8. "Initial" bulging is due to the increased tension exerted by a tumor. It is not always present, is often not excessive, and is not

likely to be followed by "consecutive" bulging.

9. "Consecutive" bulging is due to the cerebral cedema set up in normal brain tissue by trauma inflicted by the exploratory manipulations. "Consecutive" bulging far exceeds in magnitude initial bulging, and suggests the absence of a tumor of considerable size at the seat of operation.

10. In order to avoid this "consecutive" bulging, which is a most embarrassing feature of these operations, exploration should be car-

ried out in the most expeditious manner.

11. When the edges of the dural wound cannot be approximated without undue tension or without great laceration of brain substance, the gap should be closed by a graft taken from the perioranium, providing the tumor has not been found and there is reason to question the accuracy of the diagnosis.

12. When there is every assurance of a tumor being present, but it proves to be inoperable or was imperfectly localized, no attempt should be made to close the dura, as in so doing the best possible palliative effects of the operation would be counter-

acted.

13. Palliative operations should be regarded not merely as operations of propriety, but should be considered imperative whenever the tumor cannot be found or cannot be removed.

14. A statistical study of the results of the last five years is encouraging. The mortality, both immediate and subsequent, has been reduced materially. Recurrence after operations for malignant growths of the brain is no greater than after operations for malignant growth of other structures.

## RESUME OF THE OPERATIVE RECORDS.1

CASE II.—G. K.; operation May 2, 1903; osteoplastic resection of the skull; exposure and removal of cortical sarcoma; recovery from immediate effects of operation; marked improvement in patient's condition during a period of several weeks; return of the growth, with fatal termination.

Upon reflection of the osteoplastic flap and dura an area was exposed to view which, to the touch and sight, was unquestionably pathological, and proved to be the tumor. Before proceeding to remove the tumor, consideration was taken of the patient's condition, and more particularly of his circulation. If from the effect of the preliminary procedures the patient's circulation had been depressed, further manipulation would have been postponed for twenty-four to forty-eight hours, or until the circulation was re-established. In the absence of any alarming evidence of depression, the operation was continued and the tumor removed. There were no technical difficulties nor hemorrhage attending this step of the operation.

The tumor was not situated in the eentre of the arca which was exposed, but quite near the margin of the opening, so that if the opening in the skull had been a small one it is quite possible that

the tumor might have escaped the eye of the operator.

At the end of the operation the patient's temperature was 96° F., his pulse 92, and his respirations 28. The patient reacted quite promptly, and at no time did we entertain doubt as to his recovery from the immediate effects of the operation. On the evening of the operation there was complete paralysis of the right arm and leg, and aphasia; but the following morning the function of both limbs was partially restored and the patient could speak, but very indistinctly. On the fifth day a very decided improvement was observed, both in the size of his vocabulary and in the rapidity with which he could give expression to his thoughts. Generally speaking, there was a decided improvement over his condition before the operation. The headache of which he had complained so bitterly was almost entirely relieved. Occasionally he complained of a soreness in his head, but the constant distressing headache so characteristic of brain tumor had disappeared. Two weeks after the operation he left his bed, and would have been discharged from the hospital had it not been thought desirable to keep him under observation for a longer period.

CASE III.—Thomas S., aged forty-seven years; operation June 5, 1903; osteoplastic resection of the skull; subcortical tumor below the surface of the brain within the white matter; not found because of its deep situation within the substance of the brain; operative recovery;

death thirty-four days after the operation.

After preliminary closure of the carotids the osteoplastic flap and

<sup>&</sup>lt;sup>1</sup> EDITORIAL NOTE.—The clinical histories of these cases appear in full in the article by Dr. Spiller in this number of the JOURNAL.

its dura were reflected and the brain exposed. When the dura was divided the brain did not protrude, as it so often does. Its surface was inspected and several gross lesions were noted in the field exposed. These lesions were quite superficial and were not sufficiently intense to explain the symptoms. Several incisions were made into the cortex of the brain about a centimetre in depth, with a view toward exposing a subcortical growth, but the incisions were not deep enough to have revealed the tumor which was discovered at the autopsy. The flaps were replaced and the wound closed. In this, as in the former case, the patient reacted promptly from the operation, and after a slight febrile reaction, running over a period of eight days, the temperature returned to normal. During the convalescent period the patient had some convulsions, Jacksonian in type, and his left upper limb became almost completely paralyzed. He was, however, almost entirely relieved of the headache from which he had been suffering. He was transferred to Dr. Spiller's ward three weeks after the operation.

Case IV.—F. F.; operation June 23, 1903; osteoplastic resection of the skull; exposure of multiple tubercular tumors (meningitis en

plaque) of the parietal lobe; removal of growths impossible.

Several observations upon the blood pressure were made prior to the operation, and, as is now my practice, these observations were continued at intervals of not less than five minutes throughout the operation. Anticipatory of hemorrhage, both common carotids were closed temporarily. A horseshoe-shaped flap composed of the scalp was fashioned with the knife of the Stellwagen instrument and the bony flap with the drill and dental engine. Upon attempting to reflect the dura numerous adhesions were discovered between it and the cortex, but these were separated without much difficulty. Upon reflection of the dura numerous lesions, some isolated, some confluent, were revealed distributed over the entire area of the cortex which had been exposed to view. Upon introducing my index finger between the dura and exploring the cortex in all directions, I discovered more adhesions. The discovery of the latter was sufficient to warrant the assumption that the process was too diffuse and of such a nature as to render it positively inoperable. Although the manipulations had up to this time been neither prolonged nor of such a character as to inflict serious traumatism upon the cerebral tissue, yet the brain had bulged to such an extent that it became quite evident that I would not be able to bring the edges of the dura into apposition. In order to guard against the development of a hernia or a fungus cerebri, a section of perieranium was removed of a size sufficient to fill in the gap in the dural wound. Within a few minutes of the time the brain was exposed, although nothing more than a careful inspection and exploration with the finger had been resorted to, the circulation began to fail, becoming more and more depressed until the termination of the operation, when the pulse was

weak and the blood pressure alarmingly low (75). His condition for the first forty-eight hours was critical, but in the third day improved to such an extent that I began to feel more hopeful of his recovery from the operation. This reaction was only temporary, however, as ædema of the lungs rapidly developed, and on the fourth day after the operation the patient died.

CASE V.-W. C. H.; tumor of right cerebellar lobe at its union with the pons; operation July 23, 1903; eraniotomy of the eerebellar fossa; second stage of operation (opening of dura and exploration for tumor)

postponed because of patient's serious condition.

Realizing the difficulty with which all the surfaces of the cerebellum are exposed through a small unilateral opening and anticipating very free hemorrhage, not only from the scalp but from the diploic sinuses, I decided before the operation to secure a better opportunity to examine the suspected hemisphere by making a very liberal opening in the skull, one extending from one side to the other, and to control at least some of the hemorrhage by preliminary but temporary closure of the carotids. Proceeding along these lines, after the Crile clamps had been applied to the carotids I fashioned a horseshoe-shaped flap by making an incision from one mastoid process to another parallel to and 1 cm. above the superior curved line. After clamping the bleeding points in the flap, an opening in the skull was made with chisel and mallet 2 cm. below and 2 cm. from the median line. This opening was enlarged with the rongeur forceps equally in all directions until it extended above to the superior curved line and almost to the median line. A similar opening was made in the opposite side. By means of a Gigli saw the intervening bridge of bone was divided above and below and removed. With this the first stage of the operation was completed. The patient's condition at this time was such as to make it unwise to proceed to search for the tumor. From the beginning of the operation there was some evidence of impairment of the respiratory or circulatory function, perhaps both. This may or may not have been due to the anæsthesia (ether), to the loss of blood, to the fact that the position of the patient may have embarrassed respiration. At all events, he was more or less cyanosed throughout, and when the first stage of the operation was completed his pulse was very rapid (170 to 180), although his blood pressure was high (158). Immediately after his recovery from ether it was noted that he was hemiplegic. During the night his respirations were of the Cheyne-Stokes type, and there were some twitchings of the left side of the face. On the following morning, at 9 o'clock, his pulse reached its lowest rate (120), but from that time on until the patient's death, thirteen hours later, the pulse and temperature began to rise. The last registration was: pulse, 180; respiration, 24; temperature, 103.8° F.; blood pressure, 90.

# REVIEWS.

DISEASES OF THE SKIN: THEIR DESCRIPTION, PATHOLOGY, DIAGNOSIS, AND TREATMENT, WITH SPECIAL REFERENCE TO THE SKIN ERUPTIONS OF CHILDREN, AND AN ANALYSIS OF FIFTEEN THOUSAND CASES OF SKIN DISEASE. By H. RADCLIFFE-CROCKER, M.D. (Lond.), F.R.C.P., Physician for Diseases of the Skin in University College Hospital; Honorary Member of the American Dermatological Society; Membre Correspondent Etranger de la Société Francaise de Dermatologie, etc. Third Edition, revised and enlarged, with 4 plates and 112 illustrations. Philadelphia: P. Blakiston's Son & Co., 1903.

This new edition of Dr. Crocker's well-known work on Diseases of the Skin is a ponderous volume of almost 1500 pages, one-half larger than the previous one, convincing evidence of the author's industry and of the great activity prevailing in this particular field of medical research. Marks of careful and judicious revision are visible in every part of the book, which has been thoroughly brought up to date. Many new articles have been added, among the most important of which are those upon x-ray Dermatitis, Toxin Serum Eruptions, Porokeratosis, Sarcoid, Leukæmia and Pseudoleukæmia Cutis, Endothelioma Capitis, Hydrocystoma, Acne Necrotisans, Folliculitis Decalvans, and Blastomycosis Hominis. The excellent plan of putting in small type matters of minor importance has been followed in this, as in former editions.

After giving a definition of eczema, the author proceeds to make clear what forms of inflammation of the skin he includes under this term, a quite necessary step, owing to the increasing confusion among recent writers as to just what is meant by eczema. He excludes all forms of seborrhœic dermatitis as well as those due to strong irritants, but he also calls attention to the fact that certain substances which are commonly innocuous may, in certain individuals, produce a dermatitis indistinguishable from eczema, and for this and other reasons it is best to consider such inflammations among the forms of eczema. In the treatment of this oftentimes very obstinate disease turpentine internally, in 10-minim doses, is recommended as very beneficial in uncomplicated cases, care being taken to accompany it with large quantities of some diluent to avoid irritation of the genito-urinary tract. In those cases characterized

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by frequent exacerbations counterirritation over the nape of the neck or in the lumbar region, in the shape of dry heat or mustard plasters, has been found extremely serviceable by the author in

promptly relieving the itching.

In recent years the view that lupus erythematosus should be ranged among the diseases due, directly or indirectly, to tuberculosis has been gaining ground; but Crocker is not at all inclined to accept this view. He believes the affection is "primarily a vasomotor disturbance leading to an inflammation of the skin, perhaps of toxic but not of tuberculotoxic origin, especially predisposed to by a feeble blood current," with secondary microbic invasion.

Unna's view that psoriasis is but a part of the seborrheic process obtains no support from the author, who believes it is most probably due to a microparasite which finds a suitable soil only in certain individuals. This organism probably at first attacks the skin; but its rapid spread and wide distribution are best explained by supposing that it penetrates the circulation later, and is distributed by

the blood current.

The colored plates representing the principal syphilides which have been added to this edition will afford but indifferent aid in diagnosis, since they are anything but accurate representations of the lesions they are supposed to depict.

The enviable position which this treatise at once assumed upon its first appearance is easily maintained by this edition, and the student, the general practitioner, and the specialist will find it an accurate and complete presentation of the subject of dermatology, useful alike as a text-book and as a work of reference. M. B. H.

Nurses' Guide to Surgical Bandaging and Dressings. By William Johnson Smith, F.R.C.S., Principal Medical Officer, Seaman's Hospital, Greenwich. Philadelphia: J. B. Lippincott Co. London: The Scientific Press, Limited.

This is a good book badly named—one that any nurse can read with advantage. It is an excellent, handy pocket manual on surgical nursing with a title in part too modest, yet otherwise misleading. It is not with bandaging that the greater number of these pages deal, but, adapted to the needs of nurses, they contain a concise, plain, and sufficient statement of the pathology and treatment of wounds, ulcers, burns, infection, and sepsis; also of the principles and comprehensively of the practice of asepsis, antisepsis, and of special surgical nursing, and a useful chapter on splints. Of all this the cover fails to hint.

A subordinate part of the book, a couple of chapters on bandaging, through being alone honored in the title, unjustly forces comparison

with works devoted solely to this topic, notably an ideal one by an American author and from the press of the same publisher. Judged by this standard, it cannot escape harsh criticism on the score not only of incompleteness, but of insufficient illustration of the bandages described.

Had the title of this attractive little book indicated that it was a manual on surgical nursing and dressings with hints on bandaging, it would not challenge criticism, but invite praise and more than honor the promise of its back.

J. M. S.

Hyperæmia as a Therapeutic Measure (Hyperamie als Heilmittel). By Prof. August Bier, of Greifswald. Leipzig: F. W. C. Vogel, 1903.

Professor Bier has been animated by two facts in his endeavors to gain for hyperæmia a permanent place in therapeutics—that hyperæmia is one of nature's great remedial agents, for it is a well-established observation that every diseased process which the body itself attempts to cure immediately becomes surrounded by an area of hyperæmia; and that physicians should be under obligations to imitate those natural processes by which the organism is constantly

combating the inroads of disease.

He divides his book into two parts. In the first he discusses active or arterial hyperæmia, and passive or venous hyperæmia, and also the methods for the practical application of these. Hot air and vacuum apparatus, the constricting bandage, and dry cupping are described, and in a separate chapter the physiological action of dermal irritants is fully discussed. Another chapter is devoted to the description of the analgesic, bactericidal, absorbent, dissolving, and nutrient actions of hyperæmia. The second division of the book is taken up with the consideration of the methods and results of the treatment of various diseases by means of induced hyperæmia. Tuberculosis of the joints is first discussed. passive hyperæmia only can be employed, as the more pronounced active form can effect great harm. Bier recommends the procedure perfected by Tillmann, which consists of applying a constricting bandage for one hour daily sufficiently tight to induce a well-marked passive hyperæmia. There should be no pain from this, and the appearance of red blotches on the skin must be avoided. It is not necessary to bandage the parts on the peripheral side of the elastic bandage, nor is it essential to apply the constricting band immediately above the diseased joint. Thus in tuberculosis of the joints of the hands or feet the elastic bandage may be readily applied on the upper arm or the thigh. Cold abscesses should be evacuated through a small incision and the compression commenced two or 334 REVIEWS.

three days later. If abscess formation comes on during treatment, an incision is likewise made and the treatment interrupted for a few days. The fistulous tracts close quite readily and Bier has also observed the expulsion of bone sequestra during the time of treatment. Permanent fixation as a routine is not recommended, but, on the contrary, active and passive movements are begun as soon as possible. In this way Bier was able to cure cases of joint tuberculosis which experienced surgeons had designated for primary amputation.

The author of the book believes that this is the most conservative method in the treatment of joint tuberculosis, which is followed by good results without the slightest danger, and with which the function of diseased joints can be restored in a manner superior to all other conservative procedures. The method is, however, not infallible, and the condition of the patient's blood undoubtedly plays an impor-

tant rôle in the success of the process.

The acute gonorrheal inflammations have also been most favorably influenced by passive hyperæmia. Here it is necessary to apply the elastic bandage for somewhat longer periods, at least ten to twelve hours daily. The analgesic effects are particularly well marked; it is possible to move joints both actively and passively after the bandage has been in place for a short time, in which motion had previously caused most acute pain, and the wished-for sleep soon follows. In some cases the method failed, but fortunately the best results were secured in the worst cases. Bier also treated with excellent outcome instances of acute articular rheumatism and also certain inflammations of the soft parts, such as erysipelas and some varieties of phlegmonous processes, but in the latter case the author advises caution and abandons the method unless an immediate result is achieved.

Active and passive hyperæmia are both of undoubted value in the treatment of chronic articular inflammations and their consequences. In these cases the vacuum apparatus accomplishes good results. The general procedure is as follows: application of hot air daily for one hour, use of the vacuum apparatus once or twice daily for twenty to thirty minutes at a time, compression with the elastic bandage for eight to twelve hours a day, and massage and elevation

of the limb during the interim.

Treatment with hot air, because of the absorption induced by the hyperæmia, has a favorable effect in removing the ædema which often results after the healing of fractures. It was also used with gratifying results in a case of elephantiasis of the leg. Mention must also be made of the fact that neuralgic pains are benefited by active hyperæmia, and headaches, especially those accompanying an anæmia, by passive hyperæmia produced by the application of a rubber bandage around the neck.

The book is the result of most careful observation and is based

on the author's personal experiences in over one thousand cases of various diseases where positive and favorable effects were obtained by this method of treatment. In this country but few physicians have made such extensive trials of these measures, and the good results obtained by Professor Bier with this method should animate others to make further experiments and to add their knowledge gained to this interesting department of therapeutics. S. E. J.

HIGH-FREQUENCY CURRENTS IN THE TREATMENT OF SOME DISEASES. By CHISHOLM WILLIAMS, F.R.C.S. EDIN., etc. London: Rebman, Limited, 1903.

In this work the author offers "a short account of the treatment of some diseases by means of electric currents of high frequency and high potential." The main source of the account is given as from the author's own practice, supplemented by selections from "diverse journals not readily accessible to the busy practitioner." His experience with the therapeutic use of these currents dates from 1898, and in his introduction he at once arouses interest by stating that high-frequency currents "have been proved to produce extraordinary and peculiar results in the alleviation of some diseased conditions."

Certainly the uniformly excellent results secured by him in "atonic dilatation of the stomach—results far in advance of those obtainable in the same length of time by any other therapeutic agent—stir up hope that here is a form of treatment worthy of extended trial. The scope of the work includes a discussion of the different "sources of energy," of various apparatus, of the properties of the currents from physical and physiological standpoints, and lastly a consideration of therapeutic methods.

While we agree with the statement that a "certain amount of elementary electric knowledge is necessary," we cannot recommend the "elementary electrophysics" which the author gives as being either accurate or useful. The following archaic view of what takes place in a primary battery when the external circuit is closed will serve as an illustration: After describing a cell in which plates of copper and zinc are immersed in dilute sulphuric acid, he goes on to state, "When the electricity generated is allowed to circulate externally by joining the plates one notices that on each plate gas bubbles are formed from the electrolytic decomposition of the water, hydrogen and oxygen being liberated, and these bubbles interfere more or less with the chemical activity between the liquid and the metals, so that the E. M. F. and with it the tension tend to rapidly decrease; this action is termed polarization."

Now, the oxygen and hydrogen gases set free at the electrodes

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are obtained as the result of a secondary action in the dilute sulpluric acid (the electrolyte): in this, while the hydrogen is set free at the kathode, the negative ions of SO<sub>4</sub> decompose the water at the anode and combine with its hydrogen to form hydrogen sulphate and set the oxygen free; the term polarization refers to the production in the cell of an electromotive force counter to the normal one.

Under the head of Sources of Energy are discussed primary and secondary batteries, commercial electric mains, and static machines. The author's description of a static machine is not applicable to the associated cut on page 42, which is directly referred to. The really generated by induction, the difference of potential existing really generated by induction, the difference of potential existing between the disks at rest being increased by rotation.

In the chapter devoted to the description of apparatus the In the chapter devoted to the description of apparatus the elementary electrophysics, is of a nature to arouse interest. We quote as a sample from page 105: "Most of us have seen the experiment of two tuning forks tuned to the same pitch giving the same harmonic. If one be vibrated by a blow or by the fingers the second fork will start vibrating by itself and give off the same harmonic; because it is syntonous or vibrating in unison with the former, it will reinforce the sound given by the first vibrator." Now, the tone of the tuning fork is a practically simple one—i. c., a fundamental one—the overtones being inappreciable, and therefore the term harmonic is inaccurate; the second tuning fork responds to the tone of the first; it does not reinforce. This is based on the well-known principle of sympathetic vibrations.

The book will prove of interest to electrotherapeutists for the reason that it gives the opinions of a man of considerable practical experience as to the selection and use of the apparatus essential in the production of high-frequency currents.

A TEXT-BOOK OF DISEASES OF WOMEN. By BARTON COOKE HIRST, M.D., Professor of Obstetrics in the University of Pennsylvania; Gynecologist to the Howard, the Orthopedic, and the Philadelphia Hospitals. Pp. 683, with 655 illustrations, many of them in colors. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

DR. HIRST has been a consistent advocate of the opinion entertained in Germany that obstetric and gynecic surgery should always be combined. The present work, he announces in the preface, is a companion volume to the author's Text-book of Obstetrics, the two volumes covering the whole subject of gynecology." Knowing as we do his unusual experience in both branches, as well as his high reputation as a teacher and indefatigable worker, we are prepared to find his latest work a valuable addition to the literature.

The section on diseases and injuries of the vagina, includes nearly seventy pages, with no less than sixty cuts, nearly all original. We note several pages on the treatment of gonorrhea and an excellent description of the manner in which the pelvic floor is lacerated during labor. The author rightly believes that only by understanding how the injury occurs can one recognize afterward the exact nature of the lesion and the indications for operation. The detailed description of complete laceration, admirably illustrated, deserves careful study. The writer's conservatism is indicated by his adherence to the use of pessaries for cystocele. His operation for the cure of this condition is certainly an advance on the usual oval and circular methods of denndations. As he rightly says, Martin's operation "does not unite the torn muscles which should support the lower anterior vaginal wall and the urethra, and therefore it is not always permanently successful."

The writer prefers Emmet's operation for the repair of laccration of the pelvic floor, which is thoroughly described and fairly well figured. He uses silkworm-gut in all his plastic work, his experience with ehromicized catgut being less satisfactory than that of most operators. We must take exception to some of the illustrations (especially Figs. 196–198), which are more intelligible to the expert

than to the tyro.

Injuries of the cervix are profusely illustrated, unnecessarily so, the critical reader may think. We are thoroughly in accord with the statement that "whenever one is in doubt as to the suitable form of operation, it is better to decide on an amputation." Figs. 228 and 229 do not bring out with sufficient clearness the depth and extent of the denudation. Silkworm-gut is preferred for trachelorrhaphy, a conservative practice which is opposed to that of most gynecologists, who obtain equally good results with chromic gut, while the patient is spared the pain and annoyance consequent upon the removal of sutures while the perincal wound is still weak and sensitive.

The section on carcinoma is excellent. There seems to be no good reason for confusing the student by adding "malignant adenoma" as a separate variety. The paragraphs on symptomatology and diagnosis are clear and concise. Some of the illustrations, though excellent in themselves, might be dispensed with.

In common with recent views, the author prefers abdominal to vaginal extirpation, or rather the combined method, although from his description it is not clear what advantages he gains, since he does not advocate routine removal of the lymph-nodes. His lucid descriptions of surgical operations are well exemplified in the pages devoted to the technique of hysterectomy.

His conclusions with regard to prognosis after operations are fair and conservative, his immediate mortality after vaginal and com338 REVIEWS.

bined hysterectomies being 7 per cent., while four of his patients were known to be alive at the end of five years.

We are glad to note that the author still believes in the nonsurgical treatment of uncomplicated retrodisplacement, and does not reject the use of tampons in adherent retroflexion. In this he is, as ever, a safe guide to the student, who is only too apt to infer that so-called medical gynecology is a thing of the past. The descriptions of the use of pessaries and of Alexander's operation (he prefers Edebohls' method) are especially good. He seems to have had better results from plastic operations alone, with accompanying ventrosuspension, than have most of his confrères. He does not favor the recent vaginal operations of Wertheim, Freund, and others.

The section on fibromyomata and operations for their removal is ample and is beautifully illustrated. The same applies to the sections on endometritis and malignant disease of the endometrium. One is rather surprised to miss any reference to decidnoma malignum. The Fallopian tubes form the subject of Part VIII. Here, again, some of the cuts are superfluous. One characteristic illustration of each of the diseased conditions would be sufficient. The paragraph on the preventive treatment of tubal disease (pages 415–416) ought to be read by every layman, as well as physician. The author rightly believes that the palliative treatment of salpingitis should receive a fair trial before resort is had to an operation.

The section on extrauterine pregnancy is, as will be inferred from the writer's wide experience, up to date. The criticism might be offered that too little stress is laid upon the difficulties of diagnosis in many cases, as every gynecologist has experienced in his own practice. Explorative vaginal section deserves mention. The author is apparently one of the few operators who still use the old-fashioned glass drainage-tube. He states that he now rarely irrigates the abdominal cavity except to remove blood-clots after operations for ectopic gestation. The description of the operation for intraperitoneal rupture (page 441) is a model of terse writing.

Part IX., on diseases of the ovaries, leaves little to be desired. The cuts are many and original and the technique of ovariotomy

most satisfactory.

Upward of fifty pages are assigned to diseases of the urinary tract, cystoscopy and catheterization of the ureters being carefully described. Ten are devoted to floating kidney, an innovation in a work on diseases of women, doubtless in deference to the especial interest which gynecologists have taken in this subject, much to the distaste of the general surgeon. We are pleased to note that the author does not subscribe to the indiscriminate practice of performing nephropexy on slight indications, since he found it necessary to operate in only 5 out of 200 cases.

The excellent concluding chapter on the technique of gynecic

surgery in quite a model in its way, the lucid descriptions being illustrated by over 100 figures. Nothing has been omitted to furnish a safe and trustworthy guide to the beginner. It serves as a true index of the careful, conscientious work which distinguishes the author.

We have been unable in this brief review to do justice to this the latest work on gynecology. Our object has been rather to stimulate the reader to make a careful study of it for himself. While a critical reviewer might take exception to some minor defects, we are so impressed with the honest conservative tone maintained throughout, and with the fact that it is based entirely upon the personal experience and convictions of the writer, that we have only commendation for this fresh product of his wonderful industry. We have already called attention to the number and beauty of the illustrations, and to the clear, common-sense manner in which each subject is treated. While we are not prepared to admit that the present book is equal to the companion Text-book of Obstetrics, the fourth edition of which appears simultaneously with it, we have no doubt that it will achieve the same widespread popularity, which is all that the most ambitious author could desire.

H. C. C.

GYNECOLOGY. A TEXT-BOOK FOR STUDENTS AND A GUIDE FOR PRACTITIONERS. By WILLIAM R. PRYOR, M.D., Professor of Gynecology in the New York Polyclinic Medical School; Attending Gynecologist to the New York Polyclinic Hospital; Consulting Gynecologist to St. Vincent's Hospital, New York City Hospital. Pp. xvi., 380, with one hundred and sixty-three illustrations. New York and London: D. Appleton & Co., 1903.

THE preface of this excellent book indicates clearly its purpose, which is to present the subject in such a practical, dogmatic way as "a professor of gynecology in any of the colleges has to lecture." Rare diseases, bacteriology and minute anatomy, and "matters which strictly belong to other branches of medicine" are accordingly omitted.

We have not been disappointed in our favorable anticipations. Dr. Pryor has not only succeeded in writing a readable book, but one which in many respects is in a class by itself. At the outset we note with approval its division into two parts, the first, including nine chapters, being devoted to diseases and non-surgical treatment; the second to descriptions of the various gynecological operations.

In the introductory chapter on examination of the patient there are several useful practical hints with regard to the proper practice of the bimanual, important points being emphasized in large type. The illustrations are few, but satisfactory, unless we except the cut showing Trendelenburg's position, in which the elevation is extreme,

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at least for most American operators. The writer still prefers

Sims' position for examination and minor operations.

With Chapter II. (pages 14 to 68) we are introduced at once to the subject of inflammation, beginning with vulvitis and concluding with oöphoritis. The important subject of gonorrheal infection receives especial attention, in quite sharp contrast to the superficial way in which it is treated in most text-books. If space permitted we would like to quote several of the italicized sentences. The pages on gonorrheal and septic endometritis deserve careful study, since they contain an unusual amount of information condensed within a small compass.

The much-vexed subject of metritis is disposed of with less verbiage and clearer insight than is the case with most writers, for which students will feel devoutly thankful, however one may differ from the author's radical views. Peritonitis receives careful attention, twelve pages being devoted to it. With the conclusion that "peritonitis is an exponent of an infectious process rather than a

disease per se," few, if any, will dissent.

Salpingitis (another subject which has been rendered unnecessarily complicated to the student) is happily elucidated. We note in passing one of the many dogmatic statements in large type which often arrest the reader's attention and present in a few words the gist of the treatment of pyosalpinx, viz., "Suppuration in a preformed sac is cured either by removal of the sac or by its obliteration."

The concluding section on inflammations of the ovaries is another example of the process of condensation, which may not always suit the pathologist, but certainly will relieve the student's perplexity. Here again the writer shows that he holds decided views and is not afraid to express them. Referring to ovarian sclerosis (a better term, by the way, than the common "cirrhosis"), he affirms that "as the symptoms produced by such a condition are so little understood, sclerosed ovaries should never be removed unless the nterus also needs to be sacrificed."

We agree heartily with the statements that "there is no standard of gross appearance to guide the surgeon in his operations upon the ovaries," and that "few symptoms are produced by ovarian inflammations which are not easily referable to associated diseases."

Chapter III., on "Distortions and Displacements," is on the whole quite satisfactory, although some of the statements may be questioned, notably this, that "the ligaments play no part in maintaining the uterus in position until their uterine attachments are rendered tense by displacement of the uterus." The author's views with regard to the treatment of anteflexion are well known. Those on retrodisplacement are sound. Believing, as he does, that "not so much the displacement as the accompanying or causative lesions produce the symptoms," he would naturally emphasize his opinion that "there is too great a tendency in the profession to perform

operations for retrodisplacement without employing less severe methods first." This is sound teaching for the modern medical student, who is in danger of forgetting that gynecology is not

synonymous with surgery.

Sections on laceration of the cervix and perineum seem rather out of place in this chapter. The writer assigns less importance to cervical tears than other authors, not regarding this lesion as the cause of sterility, abortion, or reflex nervous symptoms, while he admits that it is a direct etiological factor in the production of cancer. In common with most gynecological surgeons, he finds that amputation is indicated much more frequently than trachelorrhaphy.

Under Chapter IV., on Diseases of the Vulva, are included diseases of the vagina and cervix, a confusing arrangement, especially as the concluding subject under cervical conditions deals with vaginismus (?). Doubtless the author will see the propriety of a rearrangement of the subject-matter in a subsequent edition, or at least a change in the heading. The important subject of pruritus deserves a place here instead of the brief mention which it receives

on page 17 under the section on Bartholinitis.

Genital fistulæ are well treated in Chapter V., though here again we note with surprise the appearance of a sub-heading on "Diseases of the Urethra and Bladder," with no less than eight pages on the ureters, a disproportionate amount of space, it would appear, in a work intended for students and practitioners, for whom the subject presents rather a scientific than a practical interest. The whole subject of diseases of the urinary tract is handled in a satisfactory manner, and we note with approval the author's original work in this field, with which the profession is already familiar.

Chapter VIII., on Cancer, is one of the best, especially the paragraphs on symptoms, which are expressed in a terse, dogmatic way well calculated to impress them upon the mind of the student. The writer thinks that the first symptom is "an increase in that leucorrhoea which the woman habitually has," bleeding being a subsequent indication. Contrary to usual observations, he does not find that menorrhagia is present. In referring to the examination of scrapings in suspected cancer of the body of the uterus he emphasizes the fact too often lost sight of, that "the positive evidence furnished by the curette and microscope is infallible, but the negative by no means shows that cancer does not exist."

With Chapter IX. we enter upon the second part of the book, where the author is entirely at home. Operations on the cervix are first considered, beginning with dilatation and curettage, and concluding with amputation. Perineorrhaphy receives careful attention. We note with some surprise that the author still uses silver wire, and does not move the bowels until the seventh day, which accounts for the statement that it may be necessary to break up hard fecal masses with a dull curette (!).

Contrary to the general opinion with regard to Pryor's radical

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methods, he is an advocate of conservative operations on the adnexa, while recognizing justly their limitations. The introductory paragraph under Chapter XV. represents a common-sense view of this much-discussed question. An interesting presentation of his opinions on vaginal section and drainage in acute salpingo-oöphoritis and acute pelvic peritonitis will be found on pages 279 and 280. The operation may strike the ordinary reader as revolutionary, but if the writer is right, "it is not only conservative, but is curative."

In Chapter XVII. there is a clear description of the author's radical operation for pelvic suppuration, with the details and remarkable results of which gynecologists are already familiar. The accompanying cuts are excellent. In the chapter on removal of the cancerous uterus the writer begins with the propositions that "no radical operation should be attempted unless the section of the tissues can pass outside the cancerous field," and that "the merits of an operation for the relief of this condition are determined by the ultimate results rather than by the immediate." He prefers the abdominal method of extirpation, since after vaginal extirpation 60 per cent. recur within the first year.

Chapter XIX. deals with various subjects, viz.: hernia, cystotomy operations during pregnancy, and a short section on the results of castration; Chapter XX. with hæmostasis, and the concluding chapter with the operative treatment of anomalies of the genitals. Following these is a "song without words," headed Chapter XXII., which includes five pages filled with cuts of

instruments, without accompanying text.

We have reviewed in a most superficial way a work which deserves careful perusal if for no other reason than it is an honest book, written by an honest man. We may dissent from some of his views and may think that his tone is often too positive and dogmatic, but we cannot deny the virility and originality which characterize his exposition of them. Looked at from a critical standpoint we cannot regard the arrangement of the book as free from faults, since the sequence is often interrupted, and there is not that natural coherence which one looks for in a scientific work. But the book must obtain prompt and widespread recognition by reason of its intrinsic excellence. The style is condensed, but never to the point of obscurity. There is no padding and no borrowing from mediaval sources, but it is essentially an exponent of personal observation. There is no doubt that the circle of readers will be larger than the author modestly hopes, for he may be sure that it will "interest even those of large experience."

When we add that the drawings are mostly original and that they are reproduced with that beauty for which the well-known firm of publishers is famous, that the text, paper, and binding are of an equally high class order, we have added enough to convince the reader that he will find the volume a distinct addition to the already formidable list of gynecological text-books.

H. C. C.

# PROGRESS

or

# MEDICAL SCIENCE.

# MEDICINE.

UNDER THE CHARGE OF

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A Case of Pentosuria.—Ernst Bendix (Münchener med. Wochenschrift, September 8, 1903, No. 36) states that although almost a decade has passed since Salkowski first taught that pentosuria is a nutritional anomaly, sui generis, very few eases of this condition have hitherto been described. This probably proceeds from the fact that many eases are overlooked on account of lack of symptoms, while others, as a result of insufficient urine examination, are called diabetes mellitus. In preparing his monograph upon this subject Bendix found only about one dozen eases in the literature: three eases by Salkowski and Jastrowitz and Salkowski and Blumenthal, two cases from Bial, one from F. Meyer, two from Brat, one from F. Blumenthal, and three cases from the Italian literature by Luzzato Reale and Colombini, the two last-mentioned cases being doubtful. In addition, three eases of Caporalis are probably not true pentosuria, but cases of glycuronic acid, leaving in all twelve cases in the whole literature. The case reported was from the practice of Dr. Auerbach, in Cologne. The patient was a merehant, aged fifty-two years. Family history good. Neither disturbances of nutrition nor nervous disease among his relatives. His parents died at about the age of cighty years. He himself, from his eighteenth or nineteenth year, suffered with his stomach. Otherwise had never been very strong. Alcoholic and venereal history were negative. About one and a half years ago lic suffered severely from influenza, with subsequent stomatitis. Convalescence was very tedious, and the patient lost much weight. At this time it was first ascertained that there was albumin in the urine and that Fehling's solution was also reduced. Since the fermentation test was negative and the urine optically inactive, the reduction of Fehling's solution was not attributed to the presence of grape-sugar. Bendix was fortunate enough at this time to find that the reducing substance was pentose. The patient was living on a mixed diet. His general nutrition was excellent. The organs of the chest were essentially normal. There was no polyphagia nor polyuria. The patient had never used alkaloids, such as morphine and cocaine. The urine had been repeatedly examined by Bendix and always showed an acid reaction, the specific gravity varying from 1016 to 1028. The albumin test was always positive, the amount varying from ½ to ½ grams pro mille.

Microscopically the cellular elements were scarce; a few leukocytes and epithelial cells were present; casts had never been found. In many of the specimens were uric acid crystals, often calcium oxalate crystals; acetone and acetoacetic acid test negative. Test for indican and diazo negative. Trommer and Fehling tests were positive and perfectly typical in the manner which Salkowski first described for peutose urine. The color change and the separation of oxydul did not occur immediately upon boiling, but only after cooling, and then very suddenly throughout the whole column of fluid. Fermentation was negative. The plane of polarized light was not turned. The phloroglucin reaction and the orcin reaction (the latter also with Bial's modification) were strongly positive. The golden yellow osazone, according to Salkowski's directions, gave the characteristic peculiarities for pentosazone (melting point,155; solubility in hot water and nitrogen content of about 17 pcr cent.). The amount of pentose in the urine varied from 0.4 per cent. to 0.6. per cent. In this case, then, it is certainly demonstrated that there was an optically inactive pentose in the urinc. Probably by analogy with Neuberg's findings it may be an arabinose.

The Influence of the Concentration of the Urine upon the Outcome of the Reactions for Albumin. - DR. BENNO HALLAUER (Münchener med. Wochenschrift, September S, 1903, No. 36, p. 1539) found that if normal human urine of ordinary concentration is evaporated on the water bath or in vacuo to one-half of its volume and then has added to it 4 per cent. of a serum containing 32 per cent. of albumin, that albumin tests performed upon this urine differ in their results from those given by ordinary albuminous urine. The boiling test gave a stronger reaction than in the case of non-concentrated urine. The Heller's reaction and the acetic-acid-potassium-ferrocyanide reaction are negative, however, with the concentrated urine. But in these cases a precipitation occurs as soon as the urine is diluted with water. The boiling test also fails with the concentrated urine if nitric acid is first added to the specimen. In this case, also, addition of water completes the reaction. He found that if the urine is still further concentrated to about one-quarter of its volume or less, even the boiling test fails to show albumin; but the addition of water restores the normal reactions. The author has tried these experiments with a great number of specimens, using serum from the horse and ox, urine from cases of nephritis, and crystallized scrum albumin. The results were always essentially the same. The potassiumferroeyanide-acetic-acid test, which has hitherto been considered a most delicate clinical test, is the first to disappear. The Heller's test often requires slightly greater concentration.

As to the cause of these phenomena, it appears that urea blocks the

Heller test, while boiling reaction is stopped by urea and neutral salts and the ferroeyanide reaction by certain salts, especially the phosphates.

Concerning the Diagnosis of Chronic Nephritis.—Schwarzkopf (Münchener med. Wochenschrift, September, 1903, No. 35, 50th Jahrg., pp. 1493, 1494) states that Nothnagel was the first to call attention to the occurrence of casts in the urine without simultaneous albuminuria. Since attention has Nothnagel observed this in patients with icterus. been turned to this subject a number of cases of "cylindruria" have been reported. Most of these were cases of drug-poisoning rather than of nephritis proper, there being a transitory injury to the kidney. The best known cases are those of Lüthje (Arch. j. klin. Med., vol. lxxiv., S. 163), who found in all of his cases, after administering salicylic acid, casts, for the most part, not accompanied with albumin. Truk's dissertation (Tübingen, 1902) gives a résumé of the literature. Schwarzkopf reports five cases considered to be chronic nephritis, in which casts occurred without albumin either for part of the time or for the whole time the patient was under observation. The author agrees with Stewart (The American Journal of the Medical Sciences, 1893) in dwelling upon the importance of remembering this in making a diagnosis in the early stage of chronic nephritis, especially in those cascs which are free from cardiac and vascular signs.

Concerning the Absence of Casts from the Urine of Patients with Nephritis.—Adolf Treutlein (Münchener med. Wochenschrift, September, 1903, 50th Jahrg., No. 35, pp. 1494–1496) concludes from his work that casts may be absent from a certain number of cases which otherwise arc typical cases of nephritis. He concludes that in these cases the casts are destroyed by lysis resulting from the action of the bacillus coli, the bacillus coli in such cases being an inhabitant of the bladder or of the pelvis of the kidney.

Is Sugar Destruction Completely Stopped after Extirpation of the Pancreas?—Luthje (Münchener med. Wochenschrift, September, 1903, 50th Jahrg., No. 36, pp. 1537-1539) points out the experimental difficulty of removing all trace of the pancreas. He calls attention to the difference between sugar formation and sugar destruction. creas certainly is concerned in the latter process. There is no ground to believe that the pancreas is the only organ concerned in sugar formation. Minkowski and others have noted that if a dog has its pancreas removed and is kept in a fasting condition the sugar disappears from the urine sooner or later. Lüthje considers this strong evidence that the sugar formed in the body by other organs is being converted. The author reports an extensive experiment in which the duodenum and panereas were removed, gastroenterostomy between the posterior wall of the stomach and a loop of intestine was performed, and the gallbladder was tied off. The experimental animal (a dog) was starved from the fifth day before operation. On the sixth day of hunger, that is, the first after operation, the percentage of sugar in the urine was 1.35, with a total of 13.5 grams of sugar. On the second day after operation, 2.25 per cent., a total of 9 grams of sugar. On the third day, 1.8 per cent., a total of 18 grams. On the fourth day after

operation, 0.4 per cent., a total of 4 grams of sngar, after which from the fifth to the tenth day sngar disappeared. The specimen of blood drawn from the femoral vein on the seventh day after operation gave strong reaction with Trommer's test and showed quantitatively 0.312 per cent. of sugar in the blood. The dog died on the tenth day. At autopsy there was a small abscess in the region of the union between the stomach and gut. Lüthje eoneludes from this that it is definitely proven that even complete extirpation of the panereas in a dog does not entirely destroy the dog's ability to consume sngar. He discusses the possible factors in sugar metabolism other than the panereas. (1) The possibility of one or more organs partially taking the place of the panereas and (2) the possibility that sngar formed in the body after panereas extirpation has a different chemical origin. He notes the striking faet that the sugar first disappears from the urine of dogs after removal of the pancreas when the dogs have established a constant starvation nitrogen value. It is to be supposed that at this time the animals are beginning to consume their own "organized" albumin and that the "reserve" albumin has been used up. Possibly sugar thus arising from albumin of cells has a different mode of breaking down. This possible hypothesis throws light on the varying amounts of sugar shown by extirpated dogs of differing degrees of nutrition and by well-nourished and cachectic human beings. It explains the faet noted in one of his experiments that after sugar had disappeared from the urine of an operated dog a small feeding of nutrose at once brought about a return of glycosuria.

Leukæmia and Tuberculosis.—Sussmann (The Practitioner, Oetober, 1903, p. 536) finds that there are only 25 undoubted eases of tuberculosis complicating leukæmia in the literature. He is inclined to the view that it is a rare complication of either the splenomedullary or the lymphatic form. He finds that, whereas tuberculosis is found to be present in from 11 per eent. to 12 per cent. of the necropsies in a series of over 7000, it occurs in only 2.4 per cent. of the autopsies in leukæmia. When the combination does oecur, it is two and one-half times more frequent in the lymphatic than in the splenomedullary form. It is six times as common in the male as in the female. The tuberculosis may be found latent and obsolete or it may supervene as a terminal infection. It may be latent and be lighted up as a result of the leukemic infection. This is the condition most commonly found. When the two diseases occur together the leukocytes are liable to diminish in number and the spleen and glands tend to decrease in size. The writer thinks that this antagonism is possibly due to the excess of nucleo-albumin and the increased phagoeytic power of the blood, both of which conditions, he claims, are present in the leukæmic patient.

Arterial Thrombosis of Gonorrheal Origin.—Norman Moore (Lancet, December 16, 1903, p. 1714) reports a ease of arterial thrombosis due to the gonococcus, and held to be the first case of the kind reported. A young man, aged twenty years, was admitted to the Manchester Royal Infirmary with gonorrhea and with early dry gangrene of the left leg. Four days previous to admission he became chilly and feverish. The day before entrance he complained of coldness and pain in the left leg. On admission the left leg was cold, waxy, pulseless, and anæsthefie

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below the tubercle of the tibia. The three outer toes showed mummification, and there was discoloration about the ankle. The left common iliac was found not to pulsate. The patient died four days after admission. The evening before death he complained of pain in the right leg, and the pulsation in the right femoral was inappreciable. The limb

below the knce was cold, pulseless, and anæsthetic.

The autopsy revealed a thrombus occluding the aorta from the renal arteries to its bifurcation. Both common iliacs and the external and internal iliacs were also filled by the thrombus. The rest of the arterial system was normal. There were no vegetations on the cardiac valves, nor were there any thrombi in the cavities of the heart. Histological examination of the thrombosed arteries showed that there was a definite acute endarteritis. Gonococci were demonstrated by Gram's method in the thrombus. No blood cultures, however, were made before or after death. Moore, nevertheless, concludes that the patient had a gonorrheal septicæmia; that an acute endarteritis was consequently set up, and that this inflammatory process caused the local development of the thrombus.

# SURGERY.

#### UNDER THE CHARGE OF

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The Operation of Gastroenterostomy, with Indications for its Performance.—Mayo Robson (Archives international de chirurgie, 1903, vol. i., No. 1) states that the operation of gastrocnterostomy is imperative in the following conditions as soon as the diagnosis is established: 1. In cases of pyloric stenosis leading to dilatation of the stomach; here gastroenterostomy provides a new outlet for the passage of the stomach contents, and thus saves the patient from starvation and death. The advantage of this operation over pyloroplasty is that in the latter operation contraction of the new orifice occasionally occurs, and this is especially apt to take place if there be active ulceration going on at the time of the operation. 2. In malignant stenosis of the pylorus; the operation has been followed by brilliant results in this class of cases and the author's experience has shown the immediate results to be almost equal to those of simple stenosis. 3. A degree of congenital stenosis is doubtless a frequent though often an unrecognized cause of dilatation of the stomach in young adults. A number of such cases have been reported and gastroenterostomy has been followed by brilliant results. 4. Congenital atresia of the pylorus, in which no passage exists between the stomach and intestine, is a defect which in all recorded cases has run a rapidly fatal course. If diagnosed early it should be treated by gastroenterostomy. 5. In chronic ulcer, with tumor of

doubtful character, too extensive or adherent for effectual removal. this operation has in some cases, where merely temporary relief only was anticipated, been followed by a complete and permanent cure. 6. In caneer or tumor of the duodenum producing obstruction to the onward passage of the stomach contents, gastroenterostomy acts in exactly the same manner as in cancer of the pylorus. As a rule, this form of disease in the second part of the duodenum is removable only with the greatest difficulty, in consequence of the important structures in the border of the lesser omentum being involved. 7. Hour-glass contraction of the stomach may be due to chronic ulcer or to cancer. If the contraction be due to simple ulceration, gastroplasty is the operation of choice, and in a number of cases the results have been excellent; but if the stricture be a long one and the thickening be very extensive, then gastrocnterostomy, in which the proximal eavity is united to the jejunum, is the better operation; but great care must be observed that the junction is not made between the bowel and the distal cavity, otherwise no benefit will ensue. It should be the operation of choice when pylorie stenosis is associated with hour-glass contraction. 8. In perigastritis with adhesions the operation of gastroenterostomy may be entirely curative; at least, it has been so in many cases; but there are some cases where the adhesions are so extensive and the secondary dilatation of the stomach is so well marked that to rest content with simply detaching adhesions would be to court failure. If the pylorus is patent, yet embarrassed by adhesions, one should always separate them, and try to avoid their recurrence by interposing the right free border of the omentum between the raw surfaces left by the gastrolysis, thus substituting a long, freely movable attachment for short binding ligaments should adhesions re-form. If, however, adhesions are very extensive and very short, dense, and firm, the operation of posterior gastroenterostomy had better be done, and this especially if at the same time there is stenosis of the pylorus or hour-glass stomach. 9. In tumor outside the pylorus, but pressing on it and causing obstruction to the passage onward of the stomach contents, gastroenterostomy may be required at the same time that the tumor is treated. The following indications apply only after the failure of systematic medical treatment: 10. In uleer of the stomach, whether acute or chronic, not yielding to medical treatment, surgical treatment is in the greater number of cases the only satisfactory method of dealing with these refractory cases, and operation should be resorted to at a much earlier period than has hitherto been the custom, and always before the patient is so far reduced by pain and starvation or the supervention of serious complieations that weakness and anæmia render any operative procedure hazardous. Before the abdomen is opened it is quite impossible to say what operation or operations will be required, and the surgeon must be prepared to adapt himself to eircumstanecs on discovering the position of the ulcer and the conditions associated with it, especially as to the presence or absence of adhesions and other complications. Gastroenterostomy acts by securing physiological rest of the stomach and, at the same time, euring the which is usually present. 11. Duodenal ulcer very o vicld to general treatment, and the author believes it is much more frequently the cause of fatal symptoms than is generally recognized. 12. In hemorrhage from the stomach or duodenum, as shown by hæmatemesis or melæna,

where general treatment has been tried or failed and where the bleeding is persisting or recurring after brief intervals, operation is advisable, with a view to find and to secure, if possible, the blecding point or points, or of performing gastroenterostomy in order to obtain physiological rest and thus to favor natural hæmostasis. 13. In persistent spasm of the pylorus, or Reichmann's disease, leading to dilatation of the stomach, pylorodiosis or stretching the sphincter may be effectual in relieving spasm and in producing immediate relief to the obstruction, but as it is apt to be followed by relapse, gastroenterostomy would seem to be the better operation. 14. Hyperchlorhydria is a concomitant of ulcer of the stomach, though it may occur apart from ulceration. As a rule, it yields to medical and general treatment, but where this fails to relieve and the life of the patient is being made miserable by constant indigestion with acid eructation, the operation of gastroenterostomy is well worth consideration, especially when in such a case it can be performed with almost no risk, for in the absence of complications such as occur in ulcer or cancer, the operations, when properly performed by an expert, ought to have no mortality. 15. Persistent gastralgia: Cases must have occurred in the practice of every physician where, although the positive signs of ulcer were absent, gastralgia of such intensity had persisted and in case of temporary relief had recurred so regularly that the patient is brought to the last stage of exhaustion by an utter inability to take food because of the pain induced by even a mouthful of solid food. Some of these cases are doubtless due to simple ulcer, but in others the absence of tenderness in the epigastrium, of rigidity of the recti, of regular vomiting, and of hæmatemesis, makes the diagnosis extremely doubtful. Even rectal feeding and absolute rest in bed do not always cure the condition, and the patient gradually loses weight and strength and lapses into a state of chronic invalidism without any positive sign of organic disease. After all ordinary means have failed, gastroenterostomy is well worthy of consideration, and in one case in the author's experience it led to an excellent result. 16. In tetany of gastric origin. The prognosis of tetany occurring in gastric dilatation is undoubtedly very serious, and, according to some authorities, death occurs in 75 per cent. of the eases. The largest mortality occurs in cases where the cramps in the extremities are associated with tonic spasms in the head and trunk museles or with elonie spasm. The author's experience would tend to show that the early surgical treatment of these cases may be followed by most beneficial results. 17. Acute gastric dilatation is one of the most serious diseases that can be encountered. But that the condition is not hopeless has been well shown by one case where lavage was followed by a cure. As yet gastroentcrostomy has not been tried as a means of relieving this condition. 18. In an exceptional case of ulcer of the stomach croding the pancreas and producing pancreatitis, with abseess draining into the stomach, a gastroenterostomy apparently saved the life of the patient by draining the very foul contents directly into the intestine. 19. Cholelithiasis may lead to perigastritis, and the contraction of bands of lymph around the pylorus may produce obstruction or kinking, thus leading to dilatation of the stomach, at the same time that the concretions lead to obstruction of the bile duets. As a rule, the condition can be relieved by gastrolysis, but where the adhesions are extensive or the thickening of the pylorus is very pronounced, the operation of gastroenterostomy may have to be performed at the

same time as the cholceystotomy. Gallstones may also lead to fistula between the gall-bladder and pylorus and the thickening of the pylorie canal may lead to obstruction, for which gastroenterostomy may be the most suitable operation, though in the eases that have come under the eare of the author the repair of the fistula in one ease and pyloroplasty in another were sufficient, when combined with eholecystotomy, to remedy the disease. 20. In atonic dilatation of the stomach, general and medical treatment, supplemented, if need be, by electrical treatment and lavage, if carried out systematically and for a sufficient length of time, usually yield good results; but in some cases, despite regular lavage of the dilated organ, well-regulated diet and general medical treatment, the dilatation persists and the nutrition of the patient and the general health become seriously impaired. In such eases the operation of gastrorrhaphy or gastroplication may be worth considering, though in certain cases gastroenterostomy may possibly be performed with advantage. The indication for operation in these cases is not so distinct as in the ease of dilatation due to pylorie obstruction, seeing that the cause is a general one; nor is the recovery after operation so rapid and satisfactory. The general health requires considerable attention at the same time that the stomach is being dealt with.

Splenectomy for Banti's Disease.—QUEEN and DUVAL (Revue de chirurgie, October 10, 1903) state that the principal characteristics of this affection are: 1. Obscure ctiology; neither alcohol, syphilis, nor tuberculosis apparently being a factor. 2. The enlargement of the spleen in all directions is the initial symptom. 3. As a result of this enlargement there develops an anemia, which is fatally progressive, but whose duration is variable, but always long, varying from three to twelve years. 4. During this anæmia the urine contains urobilin, the skin and the conjunctiva become jaundiced, and a diarrhea appears and usually lasts for some months. 5. The ascitic phase then appears. The liver is sclerosed and the eirrhosis of Laennec, which makes rapid progress, appears. 6. During the disease there is no lenkocytosis, but there is a diminution of hæmoglobin and corpuseles. 7. The morbid pathology consists in an enormous enlargement of the spleen, of from one to two kilograms in weight. Histologically there is an atrophy of the pulp and a sclerosis, with hypertrophy of the capsule and the reticulum and a partial selerosis of the Malpighian corpuscles. The liver is small, hard, granular, with a cirrhosis, presenting all the characteristics of Laennec's atrophy. 8. The bacteriological examination of the blood and the splecn is always negative. 9. The extirpation of the spleen is followed by a radical cure of the disease. If there exists a beginning hepatic cirrhosis, the splenectomy arrests its development. The authors report one ease in their own experience and six others collected from the literature in which splenectomy was followed by a complete recovery.

Adrenalin in Local Anæsthesia.—Braun (Centralblatt für Chirurgic, 1903, No. 38) states that the two most important points to be considered in the use of adrenalin for this purpose are the dose and the danger of secondary hemorrhage. As regards the dose, such a very powerful drug as it is should only be used with great eare. A dose of 1 milligram is entirely too big to be subcutaneously injected. In one case an injec-

tion of 20 e.e. of a 0.5 per cent. solution of eucaine "B." with 10 drops of the 1:1000 adrenalin solution, caused vomiting and prostration, which lasted for an hour; in several other eases this dose caused some cardiae palpitation. Hartwig and others have had some very unfavorable symptoms from this dose, and Enderlen has reported a ease where the injection of 8 eg. of eoeaine, with 8 drops of adrenalin solution, was followed by a fatal result. The best solution would seem to be one composed of hydroehlorie acid, 0.2; sodium chloride, 0.8; and distilled water, 100 parts. Then 10 c.e. of this mixture should be placed in a test-tube and heated to the boiling point, and then 1 eg. of adrenalin added, and the solution again boiled. This will give a colorless solution, in which the greater part of the salt is neutralized by the adrenalin. 2 drops of earbolic acid should be added and then the fluid should be kept in bottles holding from 3 e.c. to 5 c.e.; this solution will keep indefinitely. As regards hemorrhage, it is apparent that the anæmia resulting from the use of adrenalin is not followed by hyperæmia nor tissue paralysis, and it is not possible to seeure accurate hæmostasis in the presence of adrenalin. So care should be taken to use a very small dose of adrenalin; this markedly intensifies the duration and degree of the anæsthesia, but will not contract the arteries so as to interfere with the proper control of any bleeding that may occur.

Retroduodenal Choledochotomy.—Quervain (Centralblatt für Chirurgie, 1903, No. 40), after mentioning the work of Berg, Lane, Kocher, etc., states that though this operation is but rarely performed, still it may not be considered as a new method. After noting in detail a ease operated upon by this method with a perfect recovery, the author states that, as regards technique, the incision of the duodenum must be done very earefully and most accurate hæmostasis secured, and so any drainage to the intestinal wall will be avoided, as well as serious hemornage. Should the duodenum be turned over inward, then one should incise the choledochus at the point where it is not covered by the pancreas. The best indication of the point to cut is usually the easily felt stones. As to the choice between the retroduodenal and transduodenal methods, the former method is to be recommended in all cases where the duodenum may be easily removed. If, however, it and the pancreas are closely matted together with adhesions and further progress by the retroduodenal route is distinctly dangerous, then one should abandon all attempts at further separation and at once proceed with the transduodenal operation.

Ogston's Operation for Clubfoot.—Lauenstein (Centralblatt für Chirurgie, 1903, No. 39), after considering the question in detail, reaches the following conclusions: 1. Experience has shown that this operation is not a difficult one. 2. A careful examination with x-rays should be made in every case, and whenever possible a radiograph should be taken. 3. The amount of bone removed must be gauged by the circumstances present in each individual ease. 4. When sufficient bone has been removed, then the abnormal position can be easily and thoroughly corrected, and retention in good position can be easily obtained. 5. The after-treatment is shorter; at the end of eight weeks the child may safely be allowed to walk with a properly fitting shoc. 6. Radiographs taken subsequent to the operation show that there is

and is still more successful if forty-eight hours or less have intervened. Thus early in the infection microscopic examination of the urethral secretion shows squamous epithelial cells, leukocytes, and a few gonococci, sometimes free, sometimes in the epithelial cells, but seldom within the lcukocytes. The technique of the treatment is as follows: A 2 per cent, albargin solution is injected by means of an olive-tipped hand syringe into the anterior urethra until the patient complains of a sensation of distention. This injection is retained for five minutes and is then allowed to escape. A second injection is now given and the solution retained for three minutes. This is followed by a third, which is retained for two minutes. It is seldom that pain is complained of, but on the following night the patient may be troubled with frequency of urination. After the injection examination shows fewer leukocytes and no gonococci, and in about fourteen days the secretion entirely disappears. No complications have followed in six cases reported by the author, and in all of them equally good results have been attained.

—Therapeutische Monatshefte, 1903, No. 10, p. 508.

Hedonal.—Dr. Johann Fraczkiewicz reports that this new hypnotic, the chemical formula of which is CONH<sub>2</sub>OCHCH<sub>3</sub>C,H<sub>7</sub>, which physically is a white crystalline powder easily soluble in alcohol, ether, and boiling water, and less so in tepid water. Its taste resembles that of menthol. He uses the drug in doses of 20 grains for women and 30 grains for men. In these doses it produces in from fifteen minutes to one hour a moderately deep dreamless sleep, lasting from five to eight hours, and not followed by unpleasant after-effects, such as headache, dizziness, or ringing in the ears. During the slumber the heart action and respiration are not affected. In persons with normal kidneys the drug has a slight diuretic action, but is not so active in this regard as to disturb the rest of the patient. When there is kidney disease the diuretic effect seems to be nil. In cardiac disease the drug seems to do no harm. In conclusion, the author asserts that hedonal appears to be useful in the insomnia of hysteria, neurasthenia, marasmus senilis, and in psychoses of the milder grades. In these conditions it does no harm, even when continued for a considerable period; its diuretic effect is not cumulative. In insomnia due to pain it is useless.—Therapeutische Monatshefte, 1903, No. 11, p. 572.

Phosphorus in Psychasthenia.—Dr. Alfred Martinet asserts, as a result of his clinical observations upon phosphoric medication in psychasthenia, that in the accidental forms of the condition when taken early the treatment is quickly followed by a return of the mental processes to a normal state. In habitual psychasthenia of long standing the treatment when continued for considerable periods of time results in a progressive amelioration of the condition. In psychataxia with agitation the phosphoric medication produces a rapid aggravation of the pathological state. The phosphorus is prescribed as follows: Official phosphoric acid, 10; acid sodium phosphate, 20; distilled water, 200. Of this the patient takes at first 30 drops in a glass of water with each meal, progressively increasing the number of drops taken to 100. If there are dyspeptic or other symptoms, these are treated at the same time according to ordinary methods.—La presse médicale, 1903, No. 93, p. 805.

Lecithin -Dr. Henri Labbe believes that this drug fulfils all the indications of phosphorus and the glycerophosphates. In rickets with cod-liver oil (lecithin,1; cod-liver oil, 250) it seems to cause a cessation of the disease in from four to six months. In cases of defective growth it has also given favorable results. It is indicated in dyspepsia with phosphaturia, unless this latter is due to overfeeding, in which case, however, it may be given in small doses (3/4 to 11/2 grains) in connection with a properly regulated diet. In neurasthenia and anæmia it relieves the symptoms, increases the patient's strength and the hæmoglobin and the number of red blood cells. In tuberculosis and scnile debility it betters the general condition, but in the former disease the lesions do not seem to be modified. In diabetes, especially of the pancreatic variety, it increases the strength and weight, but does not alter the amount of sugar in the urine. In cachectic and convalescent states, except those following malaria, it is a valuable aid in the regeneration of the blood. In certain cases it acts as a heart stimulant when digitalis is useless. The continued administration of the drug is entirely harmless.—Revue de thérapeutique, 1903, No. 21, p. 721.

The Treatment of the Cardiac Complications of Rheumatism.—Dr. F. Combemale believes that if murmurs appear the cardiac condition should be closely watched for at least four weeks, during which period treatment by means of sodium salicylate should be continued; the patient should remain absolutely at rest in bed, and all excitement must be avoided. When acceleration of the pulse is noted sparteina in the following formula is prescribed: sparteina sulphate, 1; syrup of tulu, 10,000; distilled water of linden, 20,000. Of this two tablespoonfuls are given daily. Precordial pain calls for counterirritation by means of cupping or vesicants, which measures should be continued if the pain persists. If the pulse becomes irregular, as well as rapid, digitalis in the following formula: powdered digitalis leaves, 50; water, 120; fluid extract of convallaria, 30. The daily dose of this mixture is 7 to 8 drachms. Caffeine should not be employed unless myocarditis is present.—Annales de la Polyclinique de Paris, 1903, No. 11, p. 261.

Arsenous Acid in Cancerous Ulcerations —Dr. Roux de Brignolles is inclined to the theory that the topical application of arsenous acid exerts a specific action in certain forms of epitheliomatous ulcerations. In two types of cancerous lesion he has found its use followed by most happy results. These are ulcerations recurrent in the cicatrix after operation for carcinoma of the breast and cutaneous epitheliomata. Such lesions taken early and before gland involvement may be readily He believes that the curative effect of the arsenic is due to a dehydration of the cancerous tissue in the presence of fresh blood and alcohol and the combination of the drug with the cancerous elements to form an albuminate and to lessen the degeneration of the connective tissue. He uses the arsenous acid in the following formula: powdered arsenous acid, 1; ethyl alcohol and distilled water, of each, 50. this mixture the cancerous surface is painted after having been cleansed, during which process a few drops of blood, not more, must have been caused to flow. The application is allowed to evaporate and no dressing need be applied. On the next day the surface which has been treated will be covered by an eschar, which is not removed, but upon which

daily applications like the first are made until the crust becomes completely black and easily movable upon the tissues beneath. The crust may now be removed and another application made; if on the next day the resulting crust is easily movable one may be sure that the treatment is successful. If the crust is firmly fixed the treatment must be continued as before until the entire disappearance of the cancerous elements.—Gazette médicale de Paris, 1903, No. 47, p. 389.

Empyroform.—Dr. Alfred Kraus reports upon this new tar preparation, which is a condensation product of birch tar and formalin. It is used as a 1 per cent. solution with chloroform and acctone, as a paint with chloroform and traumaticin, or as a 5 per cent. ointment with equal parts of lanolin and vasclin. It is most useful in chronic cezema, relieving the itching in a decided manner, and it is even useful if there be acute symptoms. In psoriasis, lichen urticatus, prurigo, pityriasis rosea and versicolor it has given good results.—Prager medicinische Wochenschrift, 1903, No. 33, p. 419.

The Action and Therapeutic Application of Radium.—Dr. Jumon reports encouraging results from the therapeutic use of this substance in lupus. After the radium rays have been applied for five or six days the surfaces to which they have had access become reddened, and after prolonged application an appearance like that of a second-degree burn or an ulceration of the surface may be produced. The ulcers are whitish or yellowish, shallow, not indurated, painless, and slow to heal. This latter process may be facilitated by the use of dressings wet with boric acid solution. If pus germs gain access to the abraded surface suppuration may ensue. When the healing is complete, white, soft, superficial cicatrices usually result. If the application of the rays has been too short the ulccration produced is too superficial, and recurrence of the original lesion is likely to take place. On the other hand, permanent cure follows the application of "plaques" of radium of an intensity of from 5000 to 19,000 for from twenty-four to thirty-six hours. Such a treatment results in a white, pearly cicatrix, sometimes surrounded by a zone of brown pigmentation. The scar is flexible, not indurated, and unlike that produced by ordinary measures. So far as immediate result is concerned, the curative effects seem excellent; what the ultimate result will prove to be only time will tell. The advantages of the treatment are its simplicity, its freedom from pain, and the comparatively short time needed for its completion. Undoubtedly study of the subject will be followed by modifications of the technique of the use of the substance.—Revue de thérapeutique, 1903, No. 20, p. 692.

Ascites Treated by a Diet Free from Chlorides.—M. Achard reports two cases of ascites, one due to hepatic cirrhosis, the other to mitral insufficiency, where a diet in which the chlorides were reduced was followed by good results after a milk diet had failed to benefit the patients. The diet prescribed was as follows: sixteen ounces each of meat and potatoes, two ounces of rice, five ounces of sugar, and forty-five grains of salt. The first patient's weight fell in twenty-five days from 138 to 119 pounds, and so remained after an ordinary diet had been resumed; the diet prescribed was but slightly poorer in salt than the milk diet, but the diuresis due to the sugar and starches aided the

organism in the excretion of the chlorides. The aseites of the second patient increased under ordinary diet; but being put upon a diet lacking in salt her weight remained stationary for twelve days, after which the daily ingestion of 5 draehms of salt resulted in an increase of the ascites and an increase of eight pounds in weight in six days. Examination of the ascitic fluid showed a diminution in its chlorides when the patient was upon the diet lacking in salt and a rapid increase in these elements when ordinary regimen was resumed.—La semaine médicale, 1903, No. 45, p. 369.

## PEDIATRICS.

UNDER THE CHARGE OF LOUIS STARR, M.D., OF PHILADELPHIA,

AND

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Infections of the Newborn.—S. McC. Hamili, and W. R. Nicholson (Archives of Pediatries, September, 1903, p. 641) report a series of cases of infections of the newborn, and present the conclusions from their study. They do not incline to accept as pathological entities such conditions as melæna neonatorum, hemorrhagic disease of the newborn, Buhl's disease, Winckel's disease, etc. According to their observations, and in accordance with the literature, all the clinical symptoms described under these various titles may exist as manifestations of a number of different infections, the nature and severity of the symptoms depending upon the character of the infecting organism. Any classification, therefore, must depend upon a bacteriological basis.

In the six cases recorded six different micro-organisms were isolated, viz., the bacillus pyoeyaneus, the bacillus lactis aërogenes, the colon bacillus, the staphylococeus aureus, the bacillus eoli immobilis, and a streptococcus. In their complete list of cases, amounting to about fifteen, only one other micro-organism, an unclassified micrococcus, has been encountered. Various other organisms have been found in similar infections, but those most commonly encountered are the streptococcus, the bacillus coli communis, and the staphylococcus. Délestre, for instance, in thirty-seven positive cultures from infected infants, found the streptococcus fourteen times, the colon bacillus ten times, and the

staphylocoecus six times.

The post-mortem findings may be summed up in the words "congestion" and "hemorrhage," varying in degree in different eases. There is usually a considerable degree of congestion of the spleen, the mesenteric lymph nodes, the kidneys, suprarenals, liver, stomach, or intestines. Ulceration in various portions of the gastrointestinal tract has been recorded. The liver, kidneys, and the suprarenal glands may be the seat of hemorrhages. Hemorrhages into the serous cavities are common.

The bladder may contain bloody urine, and sometimes ecchymosis of

its mucous membrane is present.

The principal changes in the thoracic organs are: enlargement and congestion of the mediastinal glands, congestion in the lungs, areas of atcleetasis or pneumonia. The heart muscle is sometimes soft and frequently its vessels are enormously distended.

Histological studies are incomplete. The changes are those commonly found in infectious conditions, namely, cloudy swelling, fatty degeneration and infiltration of the liver and kidneys, in addition to the

changes resulting from hemorrhage.

Most of these infections occur in maternity hospitals, where the opportunities for the spread of disease germs are great. It is possible that the origin of these infections depends upon the presence of the various micro-organisms which bacteriological investigations have demonstrated in the air and dust of wards.

The mother's milk also has been held accountable, and not only in the presence of suppurative lesions of the breast, but also in milk from apparently normal breasts, have pathogenic organisms been isolated. The use of the same bath for several infants and the bedding together of the infected and the non-infected has resulted in conveying the infection.

Admitting the possibility of these sources of infection, the authors, nevertheless, incline to the belief that the most common medium is the poorly trained or eareless nurse. In the institutions in which they have observed these cases they have noted that they were not confined to one ward; that they have been handled by the same nurse, and that the bacteriological studies have shown the presence of different organisms in the different cases. The literature shows few examples of any one organism being held accountable for all the cases in an epidemic. These facts, they think, are against the greater frequency of air infections.

The authors believe that the eord has been given too much prominence as the point of entrance, and that the most common ports of entry are the buccal cavity, the tonsils, and the remainder of the ali-

mentary tract, and next in order the lungs.

As very little can be done in the way of treatment when infection is once established, the necessity for prophylactic measures by improving the general asceptic technique of maternity wards is of great importance.

Absolute eleanliness on the part of the attendants, eareful handling of the napkins, bed-pan, etc., separate wards and special nurses for the infants are some of the measures which would prevent, to a certain extent, these infections. The advisability of the routine practice of cleansing the infant's mouth is questioned. The recognition of any pathological condition of the breasts, such as crosions or fissures, should be a signal for the immediate withdrawal of the infant.

The Overlying of Infants —Westcott (British Medical Journal, November 7, 1903) gives some statistics upon this too frequent cause of death among infants in England.

During the last decade there were 15,009 overlain infants in England and Wales, and for the year 1902 London alone presented the shameful

mortality of 588 deaths from this cause.

The danger diminishes with the age of the infant, until at a year old the risk of suffocation by the mother is trifling.

The dead infants presented the well-known signs of death by suffocation: bluish lips, flexion of the legs and arms, clenched hands, and froth, often blood-stained, in the nostrils and mouth. Many showed undoubted marks of pressure—for example, a flattened nose. The common post-mortem findings in an infant that has died from suffocation arc: engorged lungs, sometimes ædematous; congestion of the brain and meninges, the right heart containing soft clot and the left heart empty; the pleura and pericardium showing minute ecclymoses.

Westcott deplores the fact that this habit of mothers taking infants to their own beds is so common in England, and, as it is impossible to punish parents under the existing laws, even when drunkenness is proven, he thinks it should be declared an obligation on every parent

to provide a cot or cradle for the infant's use.

# GYNECOLOGY. .

UNDER THE CHARGE OF HENRY C. COE, M.D., OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Examination of the Blood in Cases of Ovarian Cyst.—Pozzi and Bender (Annales de Gynécologie et d'Obstétrique, October, 1903) conclude a paper on this subject with the following deductions: 1. In the majority of the cases the benign or malignant character of an ovarian cystoma may be inferred from examinations of the patient's blood. 2. If the red cells are normal and the white are in the proportion of from 6000 to 8000, the tumor is benign. 3. A moderate leukocytosis with a normal number of red cells may indicate suppuration, though an increase in the white cells is noted in the case of large cysts; no positive inference can be drawn with reference to malignity. 4. With a diminution of the red cells and a leukocytosis from 12,000 to 20,000 malignant degencration may be suspected.

The presence of anæmia is a more important indication than the increase in the white cells. The percentage of hæmoglobin is of course an important aid. The writers add that blood examinations are of especial value from the standpoint of prognosis, citing two cases in which patients with marked diminution of red cells and leukocytosis

succumbed quickly after operation, without infection

Cystitis in the Female.—VEDELER (Norsk Mag. for Laegerid.; Zentralblatt jür Gynäkologie, 1902, No. 42) found only 380 patients with cystitis among 10,000 gynecological cases. He regards coitus as an etiological factor. Only 1.5 per cent. of the cases occurred in virgins, 2.5 per cent. in widows, but over 5 per cent. in married women. Of the 3 cases in little girls 2 were due to gonorrhæa following attempted coitus. Four cases resulted from the use of catheters, and in 22 cystitis

was referred to syphilis, typhoid, tuberculosis and lithiasis. In only 45 was there no accompanying disease of the urethra and genital organs. Menstruation, the climacteric, and early pregnancy seemed to have no influence upon the condition, though menstruation apparently caused an exacerbation of existing cystitis.

[We are surprised to note that so few cases were traced to the use of the catheter, which, according to our observation, is the commonest

cause of post-operative cystitis.—H. C. C.]

Plastic Operation for Hydronephrosis.—Petersen (Münchener med. Wochenschrift, 1903, No. 11) describes an ingenious operation for the relief of obstruction to the ureter following incision and drainage of a hydronephrotic kidney. The obstruction proved to be a valvular fold of mucous membrane at the entrance of the ureter. This was removed by making a longitudinal incision as in pyloroplasty and closing it transversely with eatgut sutures. The renal sac was then folded on itself at several points and the folds were sutured, so as to reduce the size of the pelvis as much as possible. The drainage of urine through the wound rapidly diminished, and at the end of six weeks the patient was discharged enred.

Parassin Injections in Incontinence of Urine.—Hock (Prager med. Wochenschrift, 1903, No. 6) reports the case of a girl, aged twenty-three years, who six years before had had a calculus removed per urethram, with resulting incontinence which resisted all treatment. After two operations for narrowing the nrethra, and one in which torsion was performed, her condition was worse than before. A second torsion gave only slight relief. Two injections of parassin (75 grains each time) were made at the neck of the bladder, when the incontinence was speedily cured. Three months later the patient again began to have dribbling of urine, and the injections were twice repeated, with permanent relief. The parassin remained unchanged at the point of injection.

Operations for Uterine Fibroid — CZEMPIN (Zentralblatt für Gynä-kologie, 1903, No. 42) reports 140 cases in which the principal indication for operation was obstinate menorrhagia. He prefers the vaginal route, saving the uterus if possible. Of the 58 vaginal operations hysterectomy was performed 17 times with no deaths. In 82 of the abdominal operations supravaginal amputation was performed 19 times with 4 deaths, and hysterectomy 44 times with 6 deaths. Two deaths were due to embolus, 5 to shock, and 3 to sepsis. There was no mortality in 19 conservative abdominal operations.

Myoperithelioma.—Gottschalk (Zentralblatt für Gynäkologic, 1903, No. 42) reports the following case, which he regards as unique: The patient, aged fifty-one years, had multiple uterine nodules, which grew rapidly and were accompanied by a constant bloody discharge. The diagnosis of fibroids with malignant degeneration was made, and the uterus was removed suecessfully. Numerous fibroid nodules were found, especially sessile submucous. The latter were covered with papillary excrescences, as well as the surrounding endometrium.

Microscopic examination showed that the growths had developed from the perithelia of the adventitia and from the deeper, rather than from the superficial vessels. In the sections of the myomata the ordinary alveolar structure of caneer was found, while in the superficial portion the pure perithelial type prevailed. The conclusion drawn by the writer was that the malignant change began in those vessels of the myoma just beneath the mucosa.

Retroflexion.—Kovwer (Zentralblatt für Gynükologie, 1903, No. 42) found 239 cases of retroflexion in 2800 gynecological cases (8.5 per cent.), of which 210 were treated. In 135 the uterus was movable, and in 75 adherent. Of the latter only 7 were operated upon, the remainder being treated with tampons. Thirty-one patients were subsequently able to wear pessaries; 25 per cent. were cured. One hundred and twenty cases of movable retrodisplacement were treated with pessaries; in 6 no treatment was necessary, and of 9 patients operated upon, 10 per cent. were cured. Only 16 out of the 239 patients (6 per cent.) were operated upon. Alexander's operation was preferred in movable retroflexion, 9 operations being recorded with 6 cures.

The writer notes that in the 5 abdominal operations for adherent retrodisplacement not a single patient was permanently relieved. He is entirely opposed to the surgical treatment of retroflexion, since by no method can the uterus be restored to its normal position. This is possible in some cases by the use of pessaries. Young girls should be

treated as little as possible.

[The frank pessimism of this writer is in striking contrast with the enthusiastic reports of most surgeons. In fact his skepticism is so avowed as to awaken the suspicion that he is an extremist. Between the views of those who denounce the use of pessaries and the opinions above expressed there is certainly a middle course which is safer than either extreme.—H. C. C.]

Treatment of Inoperable Cancer of the Uterus—Blau (Zentralblatt für Gynäkologie, 1903, No. 45) reports the result of palliative treatment in 408 cases of inoperable eancer in Chrobak's clinie. The routine method consisted in removing as much of the diseased tissue as possible with the sharp spoon and cauterizing the new surface with fuming nitrie acid or the Paquelin. The cavity is then tamponed with iodoform gauze, which is removed in four days. To promote granulation and cicatrization applications of tineture of iodine are made every two or three days. At intervals of three or four months the surface is touched with nitrie acid or a 20 per cent. alcoholic solution of bromine. Iodoform is used freely for foul discharges, with injections of permanganate of potash or ereolin. Only two patients succumbed to the operation.

342 patients were kept under observation. In three cases which presented all the elinical appearances of eaneer of the eervix (though the specimens were not examined microscopically) one patient lived for eleven years before succumbing to the disease, one was alive at the

end of nine years, and one at the end of six years.

The average duration of life after the operation was 252.3 days. Two patients now under observation were living after two to three years, four after three to four years, and one after eleven years. 109 patients (31.8 per eent.) lived over a year after operation, and thirty-three (9.6 per eent.) over two years.

Epidural Injection in Enuresis.—Kapsammer (Wiener klin. Wochenschrift, 1903, Nos. 29 and 30) made 300 injectious without a single accident. He used at first 5 cm. of cocaine solution (one-half of 1 percent.), but subsequently found that normal saline solution produced the same result. The needle is inserted at the junction of the coccyx and sacrum, so that the solution reached the roots of the cauda equina without entering the dural sac. Usually one injection is sufficient. The result of the trauma is to stimulate the nervus erigentes and to

restore the tone of the vesical sphineter.

Streptococci in the Normal Urethra.—Asakura (Zentralblatt für die Krankheiten der Hern. med. Sexualorgane, Band xiv., Heft 3) examined the secretions found in the fossa museularis in 112 apparently healthy men and found the streptococci pyogenes present in fourteen (12.5 per cent.). This fact the writer regards as of especial interest to gynecologists, since it proves that streptococci may be introduced into the vagina during the sexual aet.

The Operative Treatment of Cancer of the Uterus.—KLEIN (Münchener med. Wochenschrift, 1903, Nos. 11 and 12), after a careful study of the statistics, concludes that the percentage of cases (now 13.4 per cent.) can be still further increased by the earlier recognition of the disease by the general practitioner. To this end he should learn to diagnose the condition in its incipient stage. At the same time, the opposition of patients and their friends to early radical operation must be overcome. The laity should understand that cancer of the uterus is eurable if attacked under the most favorable conditions.

#### OPHTHALMOLOGY.

UNDER THE CHARGE OF

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AND

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The Use of a Mydriatic after the Age of Forty-five.—STARKEY, of Chicago (Journal of the American Medical Association, April 25, 1903), concludes that: "No age can be arbitrarily fixed beyond which cycloplegics must not be used, and while they are as necessary in certain cases after forty-five years as they are before, they are required in fewer and fewer cases as life advances. But since there is more danger of glaucoma in the elderly, and as mydriatics tend to increase intraocular tension, these drugs should be used with caution after the age of forty years, and in certain cases should not be used at all."

Of a number of ophthalmologists to whom questions bearing upon this point had been sent by the author, the majority agree in the main

with the above conclusion.

Periscopic Lenses.—Percival, Newcastle-on-Tyne (Arch. of Oph., July, 1903), gives the following table for the requisite eurvatures of the two surfaces of periscopic lenses. These lenses will be accurately periscopic for all eccentric vision within a solid angle of 50 degrees between —8 D. and —14 D. For powers beyond this range extreme eccentric vision will not be so good as centric vision— $e.\ g.$ , with  $a+12\ D.$  lens the vision will be distinct within a solid angle of 40 degrees—that is, 20 degrees on either side of the middle line. The index of refraction of the glass is assumed to be 1.54.

Power.						Anterior surface.	Posterior surface.
						T	6.5 D
- 1D.	•	•	•	•	•	. + 5.5 D	- 7 D ·
- 2D.	•	•	•	•	•		- 7.5 D
- 3D.	•	•	•	<b>'</b> —	•	· _	8 D
- 4D.	•	•	٠.	•	•		- 8.5 D
-5D.	•	•	•	•	•	· + 3.5 D	9 D
-6D.	•	•	•	•	•	· + 3D	
-7D.	•	•	•	•	٠	. + 2.5 D	- 9.5 D
- 8D.	•			•	•	. + 2 D	- 10 D
- 9D.						. + 1 D	10 D
- 10 D .						. Plane	10 D
12 D :						. Plane	— 12 D
14 D .						. Plane	14 D
16 D .						0.5 D	15.5 D
+ 1D.						+6D	5 D
+ 2D.	· .					. + 8 D	6 D
+ 3D.	•		•			· . + 10 D	′ - 7 D
+ 4 D .	•	•	•	•	٠	. + 12 D	8 D
+ 5D.	•	•	•	•	•	. + 13 D	8 D
	•	•	•	•	•	. + 15 D	9 D
	•	•	•	•	•	1 10 F T	- 9.5 D
+ 7D.	•	•	•	•	•		- 9.75 D
+ 8D.	•	•	, •	•	•	. + 17.75 D	- 10.5 D
+ 9D.	•	•	•	•	•	· + 19.5 D	
+ 10 D.	•	•	•	•	•	+ 21 D	11 D
+12D.	•	•	•	•	•	. + 23 D	- 11 D
+15D.	•	•	•	•	•	. + 27 D	12 D

Intraocular Lipæma.—White, of London (Lancet, October 10, 1903), reports a ease of pronounced diabetes, in which the retinal vessels, both arteries and veins, contained blood of a deep cream color, passing into pale salmon in the larger vessels. The vessels appeared a little larger than usual. The whole retina was pale.

Examination of the blood taken during life showed that, in addition to a precipitated proteid, a substance was present which, although allied to fats, was not a true fat, so that the term "lipæmia" is not strictly correct. As the diabetes improved the color in both sets of

vessels became more healthy, and, finally, quite natural.

Similar eases had been previously recorded by Heyl, Transactions of the American Ophthalmic Society, 1880; Fraser, British Medical Journal, May 23, 1903; and Reis, abstracted in the Ophthalmoscope, August, 1903.

Examination of 4608 Railroad Employes for Acuity of Vision, Hearing, and Color Perception.—MURRAY, of Seranton (Annals of Ophthalmology, January, 1903), found that of the above number 3.01 per eent. were color blind, 2.58 per eent. had weak chromatic sense, and 9.44 per eent. were in need of glasses or other means to improve their vision for distance.

#### OTOLOGY

#### UNDER THE CHARGE OF

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Ueber Horubungen Mittlest des Phonographen.—Hermann Gutzmann (Monatsschrift für Ohrenheilkunde, September, 1902) appreciates the strain upon the voice of the practitioner who undertakes exercises for the improvement of hearing. For this purpose he uses the phonograph. Tubes from the phonograph are placed in the patient's ears and all external sounds and influences excluded. The same exercise at different speeds and intensities are repeated as often as necessary.

The writer reports a case of a child, aged thirteen years, with eatarrh of the middle car as a result of searlet fever at the age of five years. Since that time the child has developed slowly, is small for her age, head small and clongated, and nose narrow and palate high. A few adenoids present in the vault, she drags her feet when walking, and is slow to learn and is easily tired. The hearing in the left car is absent. In the right car tones above B are heard, and perception of the voice impossible, except upon shouting. The mechanical control of the tongue is poor, and in the production of the vowels u, e, i, they are often changed to a, o, etc. A phonograph was obtained and six cylinders, with letters in different sequences and intensities of tone, were used. In the beginning the vowel a was heard correctly; the other vowels and most of the consonants were heard incorrectly. After fifteen days all of the vowels were heard correctly, and a marked improvement in the voice production was evident.

The writer believes that the phonograph can be a great aid in vocal exercises and saves time and also strain upon the voice.—H. D. W.

The Pathological Anatomy of the Temporal Bone.—A. Sonntag (Monatsschrift für Ohrenheilkunde, November, 1902) describes an interesting anomaly of the jugular fossa. The fossa usually extends to the level of the tympanic cavity. In this case he noticed that pressure upon the jugular vein caused a movement of the drum membrane. Investigating further he found that the bulb of the jugular was almost in apposition with the drum membrane and was covered only by inucous membrane. A large defect in the bone occupying part of the posterior half of the internal wall of the tympanum and part of the posterior wall as well was seen. The defect was kidney-shaped and about 9 mm. by 5 mm. in size. The sigmoid sinus was very far anterior. This coincides with Zuckerkandl's view that the deeper the jugular fossa the farther forward is the sinus.

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Such a location of the jugular vein is extremely important in case of paracentesis; the danger of injury and infection is evident. The blue color of some membranes has been described, but it would be difficult to recognize such a case in an acute otitis media.

A second interesting specimen was one of complete ankylosis of the malleus and incus, so that the line of the joint could not be seen. Bridges of bone passed to the inner and anterior walls of the tympauic cavity. The promontory, stapes, etc., could not be identified. The mucous membrane was thickened and in the place of the drum membrane a thin layer of bone was found occupying its position. The process was

evidently one of osteosclerosis.-H. D. W.

Ueber den Einfluss des Telephonierens auf das Gehoerorgan.-In an exhaustive review of this subject, Braunstein (Archiv f. Ohrenheilkunde, B. lix., H. 3 und 4) not only collects the conclusions of other writers, but gives the results of his own observations, which were made to include the objective and subjective examination and the reported experience of a large number of telephone operators doing from six to eight hours continuous daily service in the telephone offices in Munich. The conclusion reached is in accord with that of the majority of the writers upon this subject, whom he quotes, and is to the effect that, aside from the mechanical effect of the constant wearing of a telephone headpiece and the influence upon the general nervous system of protracted strained attention, no deleterious effects were produced; on the other hand, there were instances in which, evidenced both by the experience of the telephone operators and by subjective examinations, the hearing, for sounds of moderate intensity, was improved. operators examined, 150 had left the service; in no instance was this on account of the prejudicial influence of the telephone upon the hearing, and of those remaining in the service no one was liable to discharge because of increasing disability referable to continuance in the service.—C. J. B.

Recent Theories on Sound Conduction—Treitel (Archives of Otology, vol. xxxii., No. 5) summarizes the recent contributions to the vexed question of sound transmission through the middle car, in contradistinction to the theory of Helmholtz of the resonance value of the drumhead and the major transmission through the ossicular chain, and shows that both from a physical and a physiological basis molecule vibrations must be admitted as possible to explain both the limit of sound-perception in the human subject and the transmission through different

media to the labyrinthine capsule.

Among the first to doubt the Helmholtz theory of the function of the drumhead and ossicles was Beckman, who sees in this so-called sound-transmitting apparatus only a dampening mechanism for the very unstable labyrinthine fluid, the equlibrium of which he claims is preserved through both the fenestral membranes; in the case of the round window by its elasticity, and in the oval window by adjustment of the complicated control apparatus, the drumhead, muscles of accommodation, and ossicular chain, of which the stapes forms the terminal member. The possibility of sound transmission through the round window as a direct route, Beckman does not admit, and the improvement in hearing by use of an artificial drum-membrane he explains, not by the

transmission to the stapes of a larger segment of the sound wave, but by the weighting, artificial control effect, upon the stapes itself. In support of this idea, Beckman further cites the considerable increase in hearing by bone-conduction, with slightly decreased hearing by airconduction, in cases of acute otitis media with intact drumhead when the drumhead and malleo-incudal movements are partially inhibited

and the stapes left, supposedly, free to act.

Zimmerman is of the same opinion as Beckman as to the dampening value of the drumhead and ossicular chain, but for sounds of major intensity only, not for ordinary sound-conduction, which he claims is direct through the promontory wall for all tones, because bone is the best conductor. This proposition leaves out of view the law governing the loss of force in the translation of sound waves from one medium to another, a loss which would variously affect the partials of any compound sound wave. As an offset to this is the claim that the equilibrium of the labyrinthine fluid is maintained only through the membrane of the round window, which, because of its structure and surroundings, can only be displaced outward and cannot be regarded as a medium

for the transmission of sound waves in the opposite direction.

Zimmerman further questions the conclusions arrived at by Helmholtz and Politzer in their tests of the sympathetic movements of the individual ossicles by means of an organ-pipe tone, on the ground that the sounding body was hermetically attached to the external auditory canal and that the effects produced were those under increased air pressure; he denies, on both physical and physiological grounds, the capacity of the drumhead to react to sound of great amplitude of vibration, and regards the sympathetic vibration of the drumhead as a resonator membrane to all tones as impossible, and endeavors to explain, upon the basis of his theory of bone-conduction solely, the phenomena of lengthened bone-conduction in cases where the drumhead is absent, of improvement in hearing in such cases by application of an artificial drumhead and of paracusis.

Lucae, among others who seek to maintain the theory of sound-transmission through a middle-ear conducting mechanism, is directly opposed to the exclusive bone-conduction theory of Zimmerman, holding that while the sound waves pass directly to the labyrinth wall they are so dampened by the drumhead as to be inoperative, and that the round-window membrane is capable of responding to and transmitting sound waves, as demonstrated in the investigations of Johannes Müller.

Kleinschmidt regards the middle ear, including the mastoid eells, as an air chamber for the transmission of sound waves, the resonating effect of that cavity when filled with air under the normal condition of a patent Eustachian tube being a matter of little importance. He doubts the transmission of all notes through the ossicular chain, on account of the minimum amplitude of many of the appreciated tones, and also the ability of the accommodative muscles to act with a rapidity equivalent to the rapid succession of sounds, provided that the transmitting apparatus act as a whole. Accepting the proposition that the membrane of the round window can be set in vibration only by waves conveyed to it through the medium of the air in the middle ear, and that the stapes, with the drumhead, is actuated by low tones, this action coming later than the movement in the labyrinthine fluid due to movement of the membrane of the round window, he considers the ossicular

chain to have a dampening effect, the intrinsic muscles having no other office than that of protection of the labyrinth from excessive impulses.

Dennert, by experiments with tuning-forks vibrating in air and fluids, and Kaiser, by experiments with immersed telephones, seek to support the theory of Helmholtz, the former concluding that in air-conduction an external auxiliary apparatus especially adapted for the transmission of sound-vibration to the labyrinthine fluid is necessary, and the latter that while molecular vibration plays a part in the sound-transmission, the Helmholtz theory of mass-vibration is capable of normal acceptance.

The latest contribution to this discussion is the work of Sccchi, who maintained more than ten years ago that the only access of sound waves to the labyrinth from the air in the middle ear was through the membrane of the round window, and who further maintains, as the result of clinical observations, supplementing laboratory experiments, that the drumhead serves only as a sound check or as a passive regulator of pressure, the ossicles, under action of the intrinsic muscles, regulating the intratympanic pressure during attentive licaring and serving as a protective apparatus against the effect of major excursions upon the labyrinth.—C. J. B.

#### PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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The Dwarf Tapeworm (Hymenolipsis Nana), a Newly Recognized and Probably Rather Common American Parasite.—Stiles (New York Medical Journal, 1903, vol. lxxviii. p. 877). The dwarf tapeworm was first described in France by Dujardin, in 1845, as a parasite of the brown rat, but the term mus decumanus, which Dujardin gave to the parasite, eannot stand, since, in 1789, Gmelin used it for a different parasite. The correct name is hymenolipsis nana. About 100 cases have thus far been recorded in man, the greatest majority of them being reported from Sieily, where it is estimated that 10 per eent. of the children are infected. Before 1902 only two or three cases had been recognized in this country, but within the year the author has diagnosed the parasite in 18 infected individuals, living principally in the Southern States. Since September, 1902, the Hygienic Laboratory has examined about 3500 patients for intestinal parasites, and while "tænia solium" was not found in a single instance, and "tænia saginata" but twice, the dwarf tapeworm was discovered sixteen times. The dwarf tapeworm measures from one-fifth to slightly less than two inches in length; it has four suckers on the head and a crown of hooks. The presence of three testicles in each segment is characteristic for the genus hymenolipsis. The eggs are quite characteristic and have two distinct membranes. It

has been shown by Grassi and others that in rats the life cycle of this tapeworm takes place in the intestinal villi, and it is probable that in man autoinfection occurs, either per os and anum or by reverse peristalsis, development of the eggs through an intermediary host being unnecessary. The method of primary infection is not definitely known, but it is assumed that it occurs through the droppings of infected rats or mice in pantries and kitchens, where bread and other food may become contaminated. The dwarf tapeworm inhabits the ileum and may be present in thousands or only in very small numbers.

The symptoms produced by its presence are usually slight and may be absent altogether. Severe symptoms, however, such as persistent diarrhea, epileptiform attacks, etc., occasionally are seen. Perhaps 10 to 12 per cent. of the eases exhibit severe nervous symptoms. The diagnosis is readily made by finding the characteristic eggs in the stools. Male fern is the only drug which has met with any degree of success in the treatment of the affection. Prevention of infection is secured by cleanly personal habits and by keeping mice and rats away from food

supplies.

Localization of the Pneumococcus.-Wandel (Deut. Arch. f. klin. Med., 1903, vol. lxxviii. p. 1) reviews the literature concerning the localization of purulent infections secondary to pneumonia, and reports in detail four cases of acute pneumococcic endocarditis and three cases of pneumococcic pyæmia, with joint or heart lesions following chronic pneumococcic pneumonia. An attempt was made to trace the passage of the bacteria from the lung into the general blood stream. The fact that in pneumonia the bronchial glands are frequently swollen, and often hemorrhagic suggested that the pigmented lymph glands might act as a locus minoris resistentia for the development of the pneumococcus. In the above cases the lymph glands at the root of the hings showed more or less coal pigmentation, with swelling and softening, and in one or two instances presented small abscesses. Pncmnococci were found in great numbers in cultures and cover-slips from the pus of these absecsses, although they could only be grown in extremely small numbers from the lungs themselves. Under such conditions the normal filtration apparatus of the glands is materially interfered with, and bacteria are allowed to pass freely either into the thoracic duet or into the small bloodyessels of the lymph gland, thereby gaining entrance into the general circulation. This opinion was confirmed by microscopic examination, and the anthor believes that the origin of general systemic infections and purulent inflammations complicating pneumonia at a distance from the lungs is thus adequately explained.

A Delicate Test for the Demonstration of Bile Pigments in Urine.— Jolles (Deut. Arch. f. klin. Med., 1903, Bd. lxxviii. p. 135) has made certain modifications in the method which he formerly used to detect the presence of bile pigments in urine, and has found that this modification increases the reliability and delicacy of the reaction.

About 10 c.c. of urine are shaken in a test-tube with 2 to 3 c.c. of chloroform and 1 c.e. of a 10 per cent. solution of barium chloride. The mixture is then centrifugalized and the fluid above the sediment and chloroform drawn off with a pipette. Water is now added and the chloroform and sediment washed, the whole centrifugalized, and

the water removed by a pipette. Next 5 c.c. of alcohol are added and shaken well with the chloroform, after which 2 to 3 drops of an iodine solution are put into the mixture, and the whole filtered. If even the slightest trace of bile is present the fluid, after a few moments' standing, assumes a characteristic greenish color. If the urine is highly concentrated the reaction is best obtained by heating the mixture at 70° C. over a water bath before filtering. The reaction is not interfered with, either by indican or hæmoglobin. The iodine solution is prepared in the following manner: 0.63 gr. of iodine and 0.75 gr. of bichloride of mercury are dissolved separately in 125 c.e. of alcohol, the two solutions brought together, and the volume made up to 250 c.c. with concentrated hydroehloric acid. If the iodine solution is protected from the light in dark bottles it keeps indefinitely.

The Role of the Omentum in the Course of General Infections.—Simon (Presse Méd., 1903, T. ii. p. 726). It is already known that the omentum plays a very significant part in the cicatrization of abdominal wounds, in protecting torn or sutured peritoneal surfaces, and in walling off local infections of the peritoneum from the general cavity, but the changes in the omentum during a general infection have received but little attention. Simon found, after subcutaneous injections of lethal doses of diphtheria toxin, followed by injections of antitoxic scrum, that the omentum reacted much as the spleen does under such conditions. Diapedesis of red blood corpuscles, migration of the polymorphonuclear leukocytes from the bloodvessels, and production of large phagocytic cells were noted, while, later, accumulations of plasma cells were seen about the bloodvessels. After four or five days the reaction subsides and the omentum gradually assumes its normal appearance.

The omentum in man was found to undergo much the same series of changes in diphtheria and in variola, although the intensity of the reaction varied somewhat in the individual cases. The author concludes that the omentum does not remain inert, even in general infections, and believes that it plays a definite part in the defence of the

organism and probably in the development of immunity.

An Experimental Study of Nephrotoxins.—Pearce (Univ. of Penna. Med. Bull., 1903, vol. xvi. p. 217) says the subject of nephrotoxins has been studied in a somewhat superficial manner, particularly by the French and Italian observers, and the author in his work has repeated many of the experiments of Nefidiecf, Castaign and Rathery, Ascoli and Figari, and others, frequently arriving at results which warranted conclusions quite different from those of the authors just cited. It was found impossible to produce an autonephrotoxin in rabbits or rats by several methods employed. Ligation of the ureter or of the entire pediele of one kidney brought about only such lesions in the opposite kidney as occurred after unilateral nephrectomy, namely, a compensatory hypertrophy. It was equally impossible to produce an isonephrotoxin either by injections of serum from animals treated in the manner just described into other animals of the same species or by injecting serum produced by inoculating one animal's kidney into another animal of the same species. With heteronephrotoxins the conditions were found to be quite different. When the serum from a rabbit, which had been treated with successive doses of dog's kidney, was injected into

dogs, these animals developed a pronounced acute nephritis, evidenced by the appearance of albumin and numerous casts in the urine, together with a marked hemoglobinuria. Control experiments made by injecting dogs with the serum of normal rabbits produced no such effect. Since the heteronephrotoxie serum was hæmolytie in vitro for dog's crythroeytes it was thought that possibly a part of the renal disturbance might be dependent upon this factor; and to exclude this possibility the dog's kidneys were thoroughly washed before the immunizing doses were given to rabbits. By this means a serum was produced in rabbits which set up an intense albuminuria with numerous casts, both conditions persisting for many days, but did not give rise to hæmoglobinuria. The histological lesions in the kidneys resulting from the injections of this toxic serum consisted in an extensive granular degeneration of the convoluted tubules and a fatty metamorphosis limited almost exelusively to the loops of Henle. Granular and hyaline casts were found in the tubules of the kidney, and minor changes occurred in the glomeruli. The heteronephrotoxie serum was found to be active after heating for half an hour at 56° C. Serum prepared from the cortex of the kidney proved to be much more toxic than that obtained by injections of the medullary portions. If the liver of dogs, instead of the kidney, was used for immunizing purposes a serum was obtained which gave rise to symptoms and lesions; when injected into dogs, similar to those called forth by inoculations of heteronephrotoxic serum. In the course of the experiments several dogs were found which were the subjects of a spontaneous nephritis; and it was discovered that their blood serum was capable of giving rise to an acute nephritis when injected into healthy dogs. This effect could be produced even to the second remove. All attempts to produce chronic renal lesions by successive inoculations of heteronephrotoxic sera were unsuccessful. No immediate effect was noted upon the blood pressure following injections of heteronephrotoxic sera into dogs or of isonephrotoxic sera into rabbits. From the foregoing experiments the author believes that the correlative action of different kinds of serum upon different body cells is demonstrable and that specificity is a function of receptors and not of cells in their entirety.

#### HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.,
ASSISTANT PROFESSOR OF HYGIENE, HARVARD MEDICAL SCHOOL.

Effects of Compressed Air on the System.—Drs. Leonard Hill and J. J. R. Macleod (Journal of Hygicne, October, 1903, p. 401) have made an experimental study of the action of compressed air, which leads them to the conclusion that with proper choice of men and regulation of the shift and decompression period work can be carried on without loss of life at a depth as great as 200 feet, at which depth the pressure will exceed 100 pounds per square inch, or about 7 atmospheres. Their

experiments with animals show that compressed air above 5 atmospheres lessens the output of earbon dioxide and lowers the body temperature, and that oxygen at and above 1 atmosphere has the same effect. It is a sign of oxygen poisoning. Compressed air at 10 atmospheres is more damaging, at least to small animals, than oxygen at 2 atmospheres. increases the loss of body heat, because it is a better conductor and because it is saturated with moisture. The saturation of the air in caissons with moisture does not prevent evaporation from the body, because the skin temperature is higher than that of the air, and the wet air increases the heat loss by dampening the clothes or fur. Highly compressed air may possibly interfere with the diffusion of earbon dioxide from the alveolar air, and may, owing to increased friction, hinder the passage of air in and out of the air-tubes. The nitrogen output in dogs is not altered in any noteworthy degree by exposure to 8 atmospheres for six hours. Inflammation and consolidation of the lungs are produced by exposure to 8 atmospheres for twenty-four hours, or to 1.5 atmospheres of pure oxygen; and the higher the oxygen tension the more rapidly the inflammation ensues. It does not seem likely that inflammation of the lungs is produced with the pressures and length of exposure usual in caissons. The cause of caisson siekness is the escape of gas bubbles in the bloodvessels and tissue fluids during decompression, but recompression causes them to go into solution again, and if it is applied quickly enough the circulation rebegins. After death following rapid decompression, the bubbles can be seen in the bloodvessels, heart, rctinæ, aqueous humor, eonnective-tissue spaces, and elsewhere, and the alimentary canal is blown out with gas. The varying symptoms of caisson siekness are due to the varying seat of the air emboli. Owing to the elasticity of their tissues and to the greater facility for collateral pathways of circulation, young men escape the sickness, so that by choosing suitable men and regulating carefully the periods of compression and decompression, eaisson and divers' sickness can be avoided. Gradual decompression is most important, and, provided two hours are spent in decompression, animals can safely be exposed to 8 atmosplieres for four hours.

Factors which Determine the Local Incidence of Fatal Infantile Diarrhea. Dr. H. MEREDITH RICHARDS (Journal of Hygiene, July, 1903, p. 325) ealls attention to the faet that the various problems of infantile mortality are, with the continued fall in the birth rate, calculated to assume even greater practical importance in the near future, and that of these problems none is more in need of solution than the exact etiology of infantile diarrhoad diseases. He discusses the influence of methods of feeding, seasonal ineidence and meteorological relations, influence of social status, physiography, pollution of the soil and its effects, and concludes that fatal infantile diarrhœa is usually a form of food-poisoning; that infection usually takes place at the home; that urban conditions are chiefly hazardous from the amount of polluted soil found in the roads and yards of urban districts; that infinite care is needed if babies are to be hand-fed in towns; and that practical preventive measures should include (a) impermeable roads with efficient channelling, (b) copious swilling of roads, (c) education of mothers as to the necessity of scrupulous eleanliness, (d) the co-operative or municipal provision of specially prepared modified milk, which should be sterilized

during the diarrheal season, (e) a more efficient control of the milk trade, with special reference to the provision of cooled, approximately sterile milk from healthy cows, and (f) the provision of houses which shall be sufficiently convenient to allow of their being cleansed with the

least possible expenditure of energy.

Dr. Arthur Newsholme (Public Health, August, 1903, p. 654) asserts that much of the relative immunity from diarrhoea at Brighton, England, in 1902, was due to the rainfall, for frequent rains during the summer weeks, even though the total fall be not great, is one of the most effectual means of keeping down the diarrhoa death rate. The obvious course to pursue is, then, in time of drought, to replace the natural scavenging of rain by municipal scavenging; that is to say, by wetting the dusty streets, thus converting the dust into mud, and gathering and removing the mud, rather than merely sprinkling water to lay the dust. With regard to soil temperatures at a depth of four feet, which are regarded as an important index of the possibility of prevalence of epidemic diarrhea, he shows that Ballard's rule that diarrhea must be expected when the soil temperature at a depth of four feet reaches 56° F. is fallacious, for on June 24th the temperature was 56° F.; on June 30th it was 58.4° F.; during the second half of July it was between 60° F. and 61° F.; in August it reached 61.8° F.; on September 10th it reached the maximum, 62.6° F., and then, slowly falling, it kept above 56° F. until October 19th, when it dropped to 55.8° F.; but no deaths occurred from diarrhoea, and, contrary to the rule, the highest number of deaths from diarrhœa ocenrred three weeks later than the week in which the soil "The temperature temperature attained its mean weekly maximum. conditions were favorable to diarrhea; the rainfall prevented it. facts for the present year justify the conclusion that rainfall is more important than temperature in relation to epidemic diarrhea."

Dr. Herbert Peck, M. O. H. for Chesterfield (*Ibid.*, p. 655) is also of the same mind, for he ascribes the low death rate from diarrhæa in his district in 1902 in great part to the frequent showers. The amount of rain is of less importance than the number of showers, as is shown by a table of the rainfall for eight years. He concludes that frequent watering of the streets and roads in the more populous parts of the

district would do much to prevent deaths from this cause.

[The first to call attention to the influence of rainfall on the death rate from diarrheal diseases was Dr. E. W. Hope, who, in 1899, made known that at Liverpool during a period of twenty years the highest death rate occurred in the driest summer and the lowest in the wettest. The fourteen years in which the mean summer rainfall was 10.9 inches showed an average rate of about 50 per cent. higher mortality than the six wet years, with a mean rainfall of 13.8 inches for the corresponding months.—C. H.]

The Relation of Sulphur in Illuminating Gas to Air Vitiation.—The oppressive quality of air which is much vitiated by combustion of illuminating gas is the subject of an interesting contribution by Dr. J. S. Haldane (Journal of Hygiene, July, 1903, p. 382), who excludes the carbon dioxide produced by combustion and the attendant decrease in oxygen and increase in temperature as the causes thereof. The quantity of sulphur in ordinary gas is so small that his hypothesis that this substance is the cause of the unpleasantness may, he says, at first sight

seem improbable. English gas contains, as a rule, less than 20 grains of sulphur per 100 cubic feet, and hence, as gas forms about half its volume of carbon dioxide in burning, the products of combustion would contain less than ½ gram of sulphur per 500 litres of carbon dioxide, and this would yield about 1 gram, or 1 of a litre, of sulphur dioxide to 500 litres of earbon dioxide, or 1 volume in 1500. Hence, air vitiated by gas combustion to the extent of 30 parts of carbon dioxide per 10,000 would contain less than 0.02 sulphur dioxide, or 1 part in 500,000, which proportion is not very much smaller than Lehmann found would produce perceptible irritation of the nose and throat. Part of the sulphur is, however, in Haldane's opinion, present as sulphuric acid and in a particulate form, in which condition it has not the same specific taste as sulphurous acid, but is extremely irritating and unpleasant. In order to investigate the relation between the proportion of sulphur in gas and the unpleasantness of air vitiated by the products of combustion, he made a series of experiments, which proved that the degree of unpleasantness varies directly with the amount of sulphur, and that gas which is purified of its carbon disulphide is greatly superior, from the hygicnic standpoint, to that which is purified only of its hydrogen sulphide. Unfortunately, no process is known which will remove all of the sulphur from gas; but were it possible to do this, there would be no objection to the free use of gas for both heating and lighting and to the escape of the products of combustion into the room. He found that the air of a room in which good oil was hurned in a lamp was not noticeably unpleasant, apart from the heat, even where the carbon dioxide rose to 75 parts per 10,000; but that when gas was burned the air was distinctly unpleasant when vitiated to the extent of 30 to 40 parts of carbon dioxide per 10,000, and very unpleasant when this impurity rose to 60 parts.

The Relationship of Human and Bovine Tuberculosis.—Messrs. D. J. Hamilton and J. McLauchlan Young (Transactions of the Highland and Agricultural Society of Scotland, 1903, and Public Health, September, 1903, p. 689) undertook a series of twenty experiments designed to test the validity of the assertion that human tuberculosis differs so much from bovine that it eannot be transmitted to ealves, and arrived at the following conclusions: 1. Although human tuberculosis is probably not so virulent for the ealf as that derived from bovines, yet it can readily be inoculated upon that animal. holds good whether the tubercle inoculated be derived from tubercular lymph glands, tubercular lung, tubercular sputum, or tubercular urine. 3. It produces this positive result irrespective of whether it be introduced by feeding the animal with the tubercular material, by subcutaneous inoculation upon a peripheral part, by respiring a spray containing the bacillus, or by injection into the venous system. 4. The organs most affected are those in immediate connection with the part operated upon. 5. The lymphatic system is constantly involved in the resulting tubereulosis. 6. When administered by the mouth, tubercular sputum induces an abdominal lymph-gland tuberculosis without necessarily involving the intestine in any way. 7. When tuberculosis from a human source has been ingrafted upon a calf, it grows enormously in virulence by being reinoculated upon a second calf. S. The morphological characters of the bacillus may vary according to circumstances, and are no

guide to the source of the organism under observation. 9. The above facts go to favor the view that the human bacillus and that of bovines are identical, but modified somewhat by their environment, and directly contradict the results alleged to have been obtained by Koch and Schütz.

Prophylaxis of Malaria.—At the Eleventh International Congress of Hygiene and Demography, at Brussels, September 2-8, 1903, Pro-FESSOR A. CELLI recommended as prophylactic measures against malaria the production of artificial immunity by means of quinine, disinfection of the blood of malarial persons with quinine, mechanical protection of dwellings and of exposed parts of the body, isolation of patients, destruction of anopheles, and drainage for the destruction of their breeding places. For the production of artificial immunity, he recommended either daily doses of 5 or 6 grains of quinine (children half as much) or weekly doses of 15 grains on Saturday and Sunday evenings. The daily dose is more efficient and less unpleasant, and its action is cumulative and produces an almost complete mithridatism. The specific disinfection of the blood requires long treatment and especial care in pre-epidemic times. The Italian Government prepares quinine salts and sells them throughout the kingdom at lowest prices to apothecaries, tobacconists, and salt dealers. The peasants who work in malarial districts are supplied free of cost to themselves, the landowners being charged for it. Laborers on public works can have all they need, and the contractors for whom they work are held accountable for all deaths due to lack of supply.

The Use of Chemical Preservatives in Foods.—In a communication before the International Congress of Medicine, at Madrid, Professor Brouardel (Annales d'hygiène publique et de médecine légale, 1903, vol. xlix. p. 420) maintained that the claim made by those interested in the addition of chemical preservatives to foods, that the amounts employed are too small to produce harmful results, and that the substances used cannot be classed as harmful, because they are employed extensively as drugs in medical practice with good results, should be quite ignored and disregarded. He relates that Dubrisay has reported the finding of as much as 2 grams of salievlic acid per litre of wine, 1.25 grams per litre of beer, and 1.6 grams per kilo of butter. He regards the establishment of a maximum permissible amount of antiseptics as not worthy of consideration, since prolonged use of them may act injuriously and escape detection as the real offender. That acute poisoning has not been observed is no argument in their favor, for obviously any substance which could cause acute symptoms in the amounts used would be avoided.

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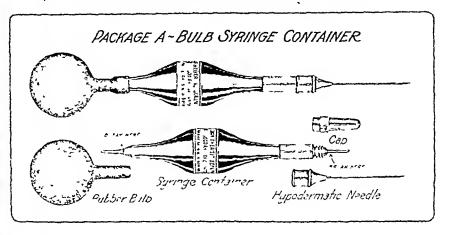
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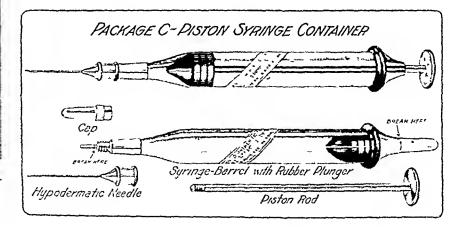
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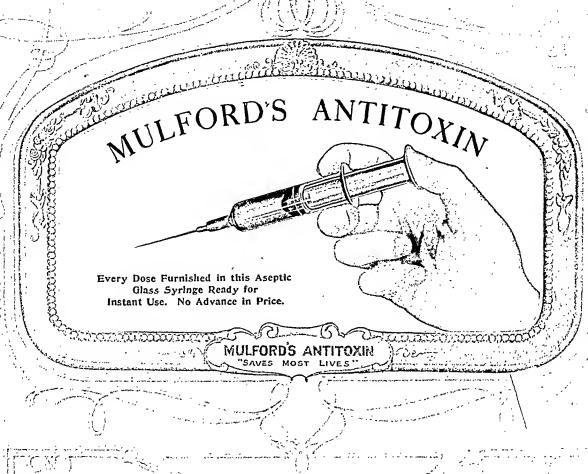
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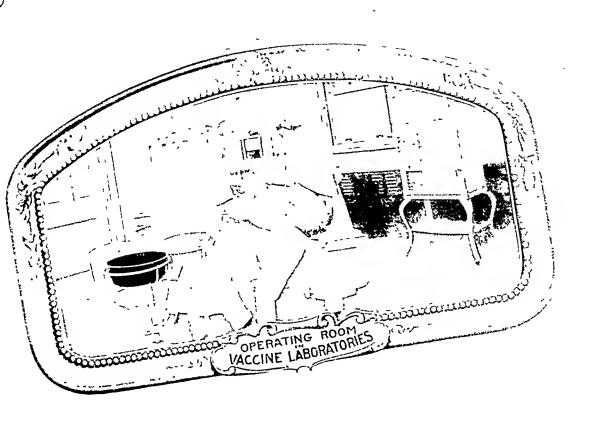
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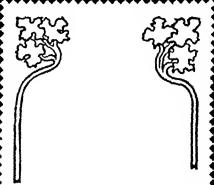
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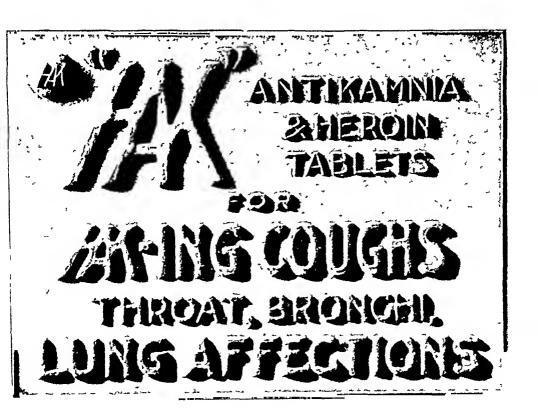
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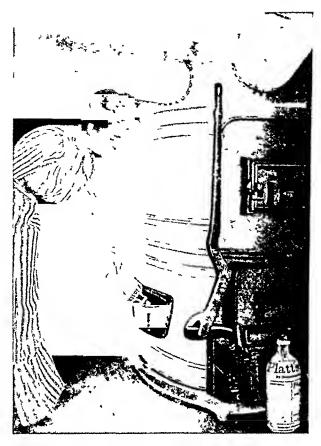
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# AMERICAN JOURNAL OF THE MEDICAL SCIENCES.

MARCH, 1904.

#### PERINEAL ZOSTER, WITH NOTES UPON CUTANEOUS SEGMENTATION POSTAXIAL TO THE LOWER LIMB.

BY HARVEY CUSILING, M.D.,
ASSOCIATE PROFESSOR OF SURGERY IN JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD.

The infrequency of herpes zoster in the cutaneous areas supplied by the sacral nerves may be gathered from Henry Head's comparatively recent tabulation in Allbutt's System of Medicine. Of the 378 eases which his exceptional opportunities have enabled him personally to observe, in seven instances only did the lesion occur in the sacral areas: once in the first, once in the second, and five times in the third segmental distribution.

If I am not at fault, the eruption which occurred in the first of the cases to be described corresponded to a lesion of the fourth (possibly of the fourth and fifth) posterior root ganglion. It is not unusual in zoster for an outlying area of hyperæsthesia to give evidence of some disturbance with the adjoining ganglia: so here there were indications that the third and second sacral were involved, the lesion, however, not being sufficient to occasion an herpetic rash. I had originally thought that the fifth sacral alone was represented by the outerop of vesicles in this ease, believing from a study of segmental cord lesions that had the fourth been involved the area would have included the posterior and lower part of the scrotum. Dr. Bardeen, however, assured me, from his reconstruction studies of the plexus in the embryo, that only in ease the fifth sacral was here of the prefixed type could it have supplied this region in the perincum.

I am unaware that a case of zoster limited to this particular territory has been described. The clinical history follows:

The patient, Mr. J. P. B., aged fifty-three years, consulted me in July, 1903, for a right-sided trigeminal neuralgia of ten years' standing. The paroxysms, having originated in the area of the N. infraorbitalis, had finally involved the other two divisions of the fifth nerve. He presented the usual pitiable appearance of those who suffer from this fearful malady in its major form.

On July 27th, under chloroform anæsthesia, the right ganglion was removed in toto. The ease proving to be an exceptionally bloodless one, the extirpation was more rapid and easy than usual. During the final steps, in elevating the superior dural envelope from the ganglion, in order to expose the sensory root, the customary escape of a small amount of cerebrospinal fluid took place. No other events seem particularly deserving of mention here. A small rubber protective drain was left in the posterior inferior angle of the incision, a provisional suture having been taken at its site.

On the following day, July 28th, the drain was removed and the provisional suture tied. There had been an abundant escape of cerebrospinal fluid. Patient comfortable, except for persisting nausea. Highest temperature 100° F. It was presumed that he would have the usual rapid and uneventful recovery so character-

istic of these cases.

July 29th (second day). Patient complains of some frontal headache, confined to the unoperated side; this was accredited to the escape of cerebrospinal fluid of the preceding day. Temperature 98.6° F.

30th. As usual on the third day the fine interrupted sutures were removed from the incision and a collodion dressing applied. There was no reaction about the wound. Complaint of some discomfort in back.

August 1st (fourth day). Severe backache, with pain running down

back of legs to ealf. Cannot be comfortable.

3d. Left frontal headache continues. Severe backache, with great sorcuess of muscles. Paquelin cautery brushed over lumbar region without giving relief. Patient can hardly move himself in bed, body or legs, without great pain. Sedatives. A few herpetic blisters forming on upper lip and ala of nose of left (sound) side (Fig. 1).

4th (seventh day). Attention called for first time by orderly to a "rash," which has appeared on the patient's perineum. Examination disclosed in the areas indicated by the accompanying diagram

<sup>1</sup> It is a point in favor of the dural origin of headache that should they occur from one cause or another after gauglion operations, provided the extirpation is complete or the trigeminal root has been divided, they are, according to my experience, invariably hemicranial and referred to the sound side. The dura, as well as the face, receives its sensory supply from the N. trigeminus, and, except for the region about the foramen magnum (pneumogastric supply). becomes an esthetic on the side of operation.

(Fig. 2) a erop of newly formed and forming vesicles confined to the right side and most numerous about the margin of the anus. Thence they spread anteriorly as far forward as the posterior edge of the serotum, and externally as far as the tuber ischii, the most external vesicle being about 6 cm. from the median raphe, with the legs in the position of the photograph. There were no vesicles on the scrotum; none on the penis; none within a radius of 3 cm. from the tip of the coceyx. Two very suspicious small red spots, which might have been broken vesicles, were present on the skin over the sacrum, just below the level of the right posterior inferior iliae spines. I could not be certain of their nature, for this was the area of the patient's maximal pain and "soreness," and it had been brushed over the day before with the Paquelin cautery.

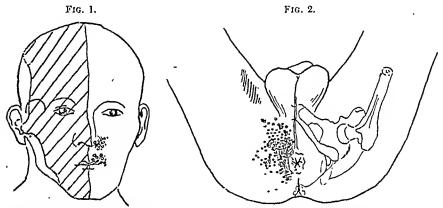


Fig. 1.—Diagram showing postoperative area of anæsthesia in Case I., with an outcrop of H. faelalis on the opposite side.

Fig. 2.—Outline sketch of area of vesiculation over perineum in Case I.

The aeling pains and soreness of the back and legs continue. These symptoms are much more marked on the right side, where the muscles and skin are tender along the back of the leg as far as the ealf.

7th (tenth day). Photograph taken (Fig. 4). Blisters over the maximal area alongside of the anus have become confluent. Pain in the back and legs much less. Can move with greater freedom.

12th. Subjective discomforts have practically disappeared. Vesieles have broken and are drying up. One small uleer left at side and slightly anterior to the anal margin. Patient sitting up with some degree of comfort for the first time, with "no pain, just soreness." There is still some tenderness present on the supporting surface while sitting; the area of cruption, however, hardly overlaps onto this area, the vesicles barely reaching the tuberosity of the ischinn in the sitting posture. When the patient stands the cruption

<sup>&</sup>lt;sup>1</sup> If, as is presumed, these were true herpetic vesicles they may be taken to represent the posterior primary division.

is hardly visible, being conecaled in this position between the mesial surfaces of the buttocks (Fig. 3).

It is quite possible to delineate the entaneous areas of disturbed sensation over the buttock and back of the right leg (Fig. 3) by gently pinching the skin; similarly the muscular areas of soreness by pressure. The entaneous areas, although tests with the hair æsthesiometer and graded thermic tests show that there is considerable actual tactile and thermic hypesthesia, nevertheless are hyperæsthetic to painful stimuli, pressured in the presentation of the right half of the scrotum, as well as the territory shown in Fig. 3 over the gluteofemoral region. The area of maximal tenderness, both surface and deep, lies over the sacrum, just below

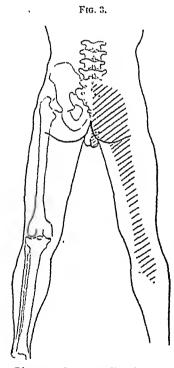


Diagram of sensory disturbance in Case 1., with patient in an upright posture, showing the few vesicles at the edge of the buttock, which were visible in this attitude. Shaded area indicates the hyperesthetic zone, presumably S. II. and S. III.

the level of the posterior iliae spine. The muscles underlying the entire territory are tender ("sore") on pressure well down on to the calf. No evidence of disturbed sensation of the sole of the foot could be made out. The body temperature, which has been slightly subnormal since the third day, has again reached the normal point.

The deep reflexes are present and active both at the knee and ankle. They are equal on the two sides. A normal plantar reflex is easily elicited on either side. No eremasteric reflex could be brought out, though the vermicular movements of the dartos were active.

13th. Continued improvement. Examination confirms observations of yesterday. Hyperæsthetic area marked out again by pinching the skin. No cremasteric and no anal reflex could be elicited on either side. Sensory symptoms remain the same, but the patient complains of less subjective discomfort.

24th (twenty-eighth day). For the past week the patient has been absolutely free from subjective sensations. There is no trace at present of the

hyperæsthetie zone corresponding to the second and third sacral areas. The sears of the eruption are not tender. Some diminution of thermie sense alone persists in patches over the area occupied by these scars. The anal and cremasteric reflexes have returned.

The patient has gained seventeen and one-half pounds in weight since August 10th (fourteen days).

In my personal series of twenty cases of Gasserian ganglion extirpation, this is the second time in which an herpetie eruption has occurred as an evident sequel of the operative procedure. The earlier case consequently may be deserving of mention here, for, although the eruption of vesieles was entirely confined to the areas of the trigeminal and eervical nerves, a bilateral hyperæsthesia of the fourth and fifth sacral territories accompanied it. In the light of the more recent observation, I cannot believe otherwise than that the process was occasioned by some disturbance with the lower sacral posterior root ganglia, which stopped short of causing an herpetic eruption.

The case in brief is as follows:

Case II.—The patient, Alexander D., aged thirty-cight years, entered the Johns Hopkins Hospital in January, 1900. He was suffering with a severe right-sided trigeminal neuralgia, which had thrice recurred after peripheral operations, and had finally involved all three divisions of the nerve. A suboecipital extension was also present.

On January 15th the right ganglion was removed in toto. The extirpation presented no great difficulties, although the case was a bloody one. The wound was elosed without drainage, as the oozing

eeased after removing the ganglion.

His convalescence promised to be without incident. The temperature registered 100° F. the day ofter the operation, its highest point. The sutures were removed from the wound on the third day. It apparently was healing without reaction. He was allowed to be

up and about the following day. Temperature normal.

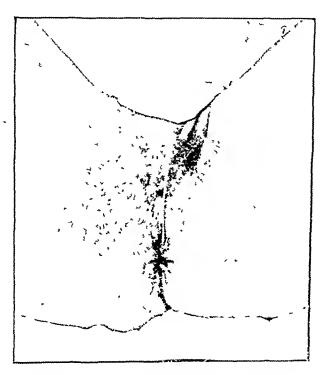
Five days later—that is, on the ninth day after operation, he exposed himself in a chilly bath-room during his morning ablutions and sneezed violently three times. He immediately eried out with severe pain in the head, spine, and down the back of his legs. He had a chill, during which his temperature rose to 104.8° F., but fell

again after a few hours to normal, where it remained.

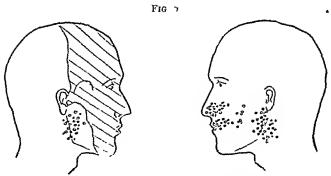
In forty-eight hours an extensive crop of herpes had developed, with a distribution as follows (Fig. 5): On the left side of the face, chiefly on the nose, upper lip, and cheek (second division of the N. trigeminus), and also on the neek overlapping the angle of the jaw (N. aurieularis magnus, third or second cervical) were large areas of closely placed vesicles, many of which subsequently became confluent. On the right side also was a symmetrically placed patch (cervical distribution) near the angle of the jaw, entirely outside of the postoperative area of anæsthesia (Fig. 5). Of course, no eruption of the nature of true zoster could occur in the right trigeminal area. In addition to this extensive bilateral outcrop of vesicles, with its attendant discomforts about the head, pain and paræsthesia were

complained of at the opposite pole of the body, and on examination it was found that a symmetrical area (Fig. 6), including the margin

Tig. 4



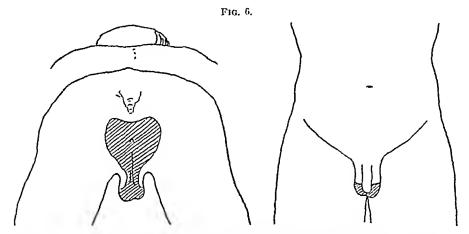
Photograph of perincal zoster in Case I , showing condition of cruption on the third day after its appearance



CASE II —Distribution of facial and bilateral corvical herpes—Note that the postoperative anæsthetic area remains free, indicating that the other cruptions presumably originated from lesions in the posterior root ganglia (cervical and trigeminal).

of the anus, perineum, and lower portions of the scrotum, was hyperæsthetic to painful stimuli, while slightly hypæsthetic to delicate tactile (hair æsthesiometer) and thermic stimuli. Over this area the patient experienced a most disagreeable sensation of formication. An herpetic rash was anticipated, and though it did not materialize, I nevertheless considered that the condition was resultant to a lesion of the corresponding posterior root ganglion (herpes zoster, without the cruption).<sup>1</sup>

Some tenderness of skin and muscles on pressure existed over the buttocks and down the back of the legs, extending on one side as far as the sole of the foot. These symptoms all cleared up in the course of a few days, together with the disappearance of the herpetic cruption on the face. It was necessary, however, to catheterize the patient for some time after the onset of the attack.



Bilateral hyposthetic area in Case II., considered to represent a lesion of posterior root gauglia (S. IV.), which did not suffice to cause residuation of the skin.

There is much dispute over the relationship between herpes zoster and the herpetic eruptions which occur so often, particularly in febrile states, about the margins of the lips or nose or of the prepuce. Some believe that the causal agent in the two conditions is the same, though I think the majority are of quite a contrary opinion.<sup>2</sup>

Bilateral zoster, of course, is exceptionally rare, and for it to appear at the same segmental level on the two sides is practically unknown; consequently many will consider the facial cruption in this, as well as in the previous case, to have been of the nature of H. febrilis seu labialis, which is so commonly bilateral. If this is so, there can be little doubt, from these observations, but that the

<sup>1</sup> Although "herpes zoster" would be an absurd misnomer for such conditions, there being neither a rash nor a girdle-like distribution, James Mackenzie (Some Points Bearing on the Association of Sensory Disorders and Visceral Disease, Brain, 1893, vol. xvi. p. 314) nevertheless contends that essentially the same disease of the posterior ganglia may be present without producing vesiculation of the skin, the pain and sensory disorders alone indicating the nature of the lesion and its site.

<sup>&</sup>lt;sup>2</sup> Those inclining to one or the other view are cited in Spitzer's recent Sammel-Referate, Neuere Erfahrungen über den Herpes Zoster, Centralblatt f d. Grenzgebiete d. Med. u. Chir., 1901, Bd. iv. p. 548.

presence of the Ganglion semilunare, which is the cranial homologue of the spinal posterior root ganglia, is essential for the production of herpetic eruptions of this nature, since in both cases the cutaneous area rendered anæsthetic by the extirpation remained free from vesiculation.

It is curious that these two cases should both have presented symptoms not only of disturbance in the intact and remaining Ganglion semilunare (mild in the case first reported and severe in the latter one), but also of disturbance with the posterior ganglia of the most remote sacral segments (severe in the first case and mild in the latter one). It would almost seem that gravitation must have played a part in bringing about a deposition of the infective agent, whatever it may have been, in the caudal portion of the meningeal sac, and the anatomical position of the terminal sacral ganglia (Fig. 7) at the verylowermost part of the sac would perhaps favor such a view. It seems unlikely that there should have been a different ctiological factor at work in bringing about the trigeminal and the sacral processes.

On Sensory Segmentation Postaxial to the Lower Limb.

As is well known, several methods may be utilized for the approximate determination of the cutaneous areas presided over by the individual units of the spinal cord.

ANATOMICAL. In the first place, by dissection the nerves may be traced from the cord to their finer entancous ramifications. For those parts of the body in which the successive trunks retain the semblance of their primitive segmental character, this anatomical method presents no great difficulties. It is quite otherwise, however, with the nerves destined to supply the limbs, since by their fusion into a plexus they become complicated to a most puzzling degree. This is true, even in the early embryo, for, as Dr. Bardeen's morphological studies have demonstrated, the plexuses have begun to form long before the nerves have reached their destination in the skin covering the budding extremity.

Careful anatomical dissections, such as those of Paterson,<sup>2</sup> Eisler,<sup>3</sup> and others, serve to show the great variations as regards their spinal roots which exist for the lumbosacral nerves, and how difficult it is by the dissection method to obtain any clear conception of cutaneous segmentation such as would be of use for clinical purposes.

<sup>&</sup>lt;sup>1</sup> From an etiological standpoint I am unable to account for the cruption in these cases. Presumably there was an infective agency of some kind. In the first case, however, the temperature remained normal or slightly subnormal during the entire period of cruption. In the second case an alteration in the temperature curve like that of a malarial paroxysm took place. Unlike the malarial chill, however, there was an associated rise in leukocytes, from 4500 to 22,000. Both the leukocytosis and pyrexia quickly returned in a few hours to their normal points.

<sup>2.</sup> The Origin and Distribution of the Nerves to the Lower Limbs, Journal of Anatomy and Physiology, 1893-1894, vol. xxviii, pp. 84 and 169.

<sup>&</sup>lt;sup>3</sup> Der Plexus lumbo-aeralis des Menschen, Halle, 1892.

FIG. 7.

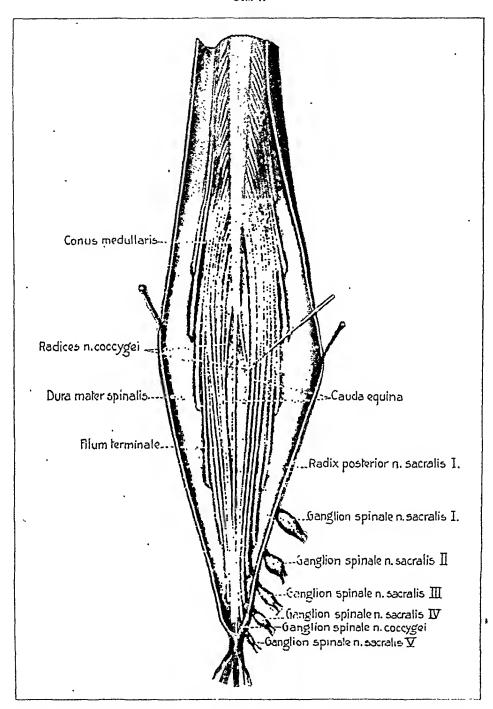
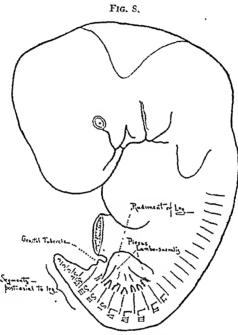


Diagram borrowed from Toldt's Anatomisches Atlas, 1903, ishowing the situation of the lowermost posterior root ganglia at the extremity of the meningeal sac.

In the region caudal to the extremity with which we are dealing, there is, to be sure, a return again to a somewhat more simple type of root distribution. In the average individual, that is one in whom the plexus is neither placed higher nor lower in relation to the limb (prefixed or postfixed, according to Sherrington's terminology) than the normal type, it may be said that the second sacral is the lowest of the roots to enter completely into a leg distribution. The segments below this level (third sacral to coccygeal) supply the terminal or caudal end of the body, where, uncomplicated by the growing ex-



Diagrammatic outline of a four and one-half weeks' embryo, showing the segments (S. III,—coeeygeal) postaxial to the rudimentary hind limb. The nerve roots (LI. to S. II.) form the lumbosaeral plexus, destined for the most part for distribution in the leg. The sensory elements of the four lower mintomes (S. III.—coceygeal) are destined for the parts about the cloaca, penis, scrotum, perineum, anal region, and buttock. For comparison with adult distribution see Fig. 10. (Sketch adapted from Bardeen and Lewis, American Journal of Anatomy, vol. 1., No. 1, Plate III.)

tremity, their cutaneous areas present a zonal distribution running clearly from mid-dorsum to mid-venter. The anatomical arrangement is not quite so simple, however, as in the trunk above the limb, for these lower nerves do enter into a certain plexiform arrangement, the so-called plexus pudendus (anat. nomen.) or plexus finalis trunci (Renz), and beyond the stated fact that the skin over the genitalia, perineum, buttock, and ischioanal region is supplied usually by segments below the second sacral, there is but little attempt anatomically to indicate any clear zonal distribution.

In the upright attitude of the adult, all evidence that the original

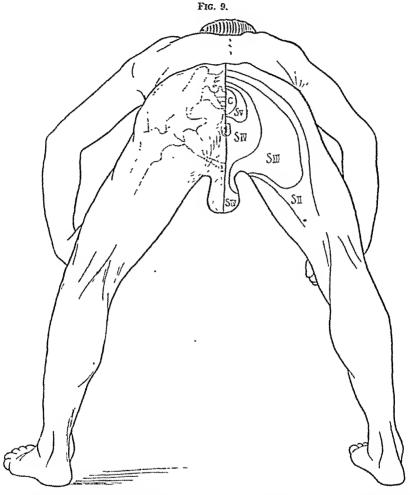
situation of these parts was postaxial to the limb is lost, and only by a morphological comparison with their primitive simple arrangement is it possible to obtain a clear idea of their subsequent configuration. In very schematic fashion I have endeavored to indicate by the accompanying sketch of a four weeks' embryo, kindly supplied by Dr. Mall, the position of these lower cutaneous zones before the growth of the leg led to their distortion (Fig. 8).

Physiological. Secondly, the experimental method, although exact in many ways, nevertheless presents serious drawbacks, chiefly owing to the difficulty of interpretation of sensations in their transference from animals to man. Were it not for this factor, the physiologist would be able accurately to delineate the cutancons strips of each segment by a procedure which Head has appropriately called "the method of remaining æsthesia." This method, first practised by Sherrington, consists in the division of the posterior roots of two or more segments, both above and below the particular zone which is to be studied. Thus, there should remain an æsthetic zone of skin with intact nerve supply in the midst of an anæsthetic field, and with no confusion from overlapping. Owing to this functional overlap of neighboring segments, as Sherrington first demonstrated, the division of a single posterior root does not suffice to produce a strip of "resultant anæsthesia." The subject could not, therefore, be studied in any such simple way. Charts, furthermore, based upon observations from lower animals, are not easily transferable to the cutaneous fields of man, and there is considerable evidence, as Head and Thorburn have pointed out, that the sensory fields of the spinal segments are more sharply defined than are the root areas with which experimental physiologists and anatomists have chiefly concerned themselves.

CLINICAL. 1. Traumatic Paralyses. A third and possibly the most satisfactory method of delineating at least the upper margins of the several segmental areas occurs in association with cases of spinal injury, in which a clean-cut, total, transverse lesion of the cord has occurred. By the combination of a sufficient number of such cases, especially when the level of the lesion has been determined by a post-mortem study, the sensory zones for the individual segments may be accurately mapped out. The areas thus determined and figured by Allen Starr, 1892; Thorburn, 1893; Kocher, 1898; and Wichmann, 1900, furnish data for the best-known and most earefully represented charts of this kind (Fig. 9).

It is, however, very unusual for traumatic injuries to pick out the tip of the conus medullaris, enclosed and protected as it is by the powerful lumbar vertebra, without injuring at the same time the neighboring strands of the cauda equina, thus giving a picture a segment or two higher than the level of the actual cord lesion. It is very rare, on the other hand, for cases of injury limited to the cauda equina and occasioned by sacral injuries to occur low enough

to involve the roots below the third sacral and to leave those above unaffected.<sup>1</sup> Thus Thorburn<sup>2</sup> gives in his diagram no segmentation below the third sacral, remarking that "the fourth sacral and sub-



A representation of the sacral areas as indicated by the diagrams of Starr, Thorburn, Head, Koeher, and Wichmann. The corresponding zones in each figure have, for case of comparison, been shaded in a similar way. It will be noted that there is considerable unanimity in the configuration at the area accredited to the third sacral (S. III.). Wichmann's figure alone falls to indicate the "saddle-shaped" form, though his context mentions it as characteristic of this zone.

jacent roots are not indicated, being placed too low down in the perineum for representation in these sketches" (Fig. 9).

<sup>1</sup> Cases of pelvic operation by the sacral route (Kraske), in which by resection of the coccyx and oblique division of the lower part of the sacrum including, at least on one side, the foramina of exit of S. V. or IV., or even in some cases S. III., seemingly would offer favorable opportunities for the study of the sensory areas of the corresponding roots. I have as yet been unable to make any satisfactory observations on patients with such surgical lesions.

<sup>\*</sup> The Sensory Distribution of the Spinal Nerves, Brain, 1893, vol. xvi. p. 255, and elsewhere.

The lowest area represented in Koeher's otherwise remarkably perfect series is the third saeral and one, according to my interpretation, in which this territory possibly is indicated only in part, together with the fourth and lower areas, so that its representation is somewhat larger than the actual distribution of the fourth saeral as usually indicated.

Wiehmann<sup>2</sup> has adopted in his diagram a spectral color scheme, which, when familiarized, is in many respects useful for purposes In the extremities, however, he has allowed for of orientation. variation and overlapping to such an extent that the separate segmental units are not as clearly outlined as his individual cases seemingly would justify; consequently, in these areas (second lumbar and second sacral, inclusive) the diagram is confusing. This is not the ease, however, with the zonal arrangement of those segments of the trunk which have not been distorted by the outgrowth of the limb. Following Renz, he includes, under the heading Plexus finalis trunci, the third, fourth, and fifth saeral and the eoecygeal segments, whose areas all lie eaudad to the lower extremities. The third saeral alone overlaps slightly on the extremities, so that its area of representation is no longer eircular like those which lie below it, but has become distorted into the familiar figure ("saddle-shaped") noted by many observers as resembling the imprint which the buttock makes upon a chair. This configuration, though alluded to in his context and apparent in the sketches of his individual cases, he has failed to indicate in his combined diagram (Fig. 9).

Starr's<sup>3</sup> figure, although antedating those of Kocher and Wichmann by several years, and in spite of its deficiencies to which many have ealled attention, nevertheless, seems to me, so far as the scheme of representation of the three lower areas goes, to be much the more satisfactory. In it each of the sacral segments on the buttock, starting below at the fifth, successively encircles the area caudad to its own representation, and thus the principle of segmentation posteriorly on the trunk is more or less graphically indicated, and the effect which the growth of the limb has had in distorting the original circular strips becomes intelligible. Whether or not a successive diminution in the diametrical width of these areas on the buttock, from the first sacral tailward, is clearly demonstrable, I cannot from personal observations take a positive stand, but my impression, in accord with Thorburn and Starr, is that the diameters do so diminish.

2. Referred Pain and Zoster. In addition to those mentioned above a final method remains.

The demonstration by Mehlis (1818), that a herpetic eruption

<sup>&</sup>lt;sup>1</sup> Die Verletzungen der Wirbelsänle zugleich, also Beitrag zur Physiologie des menslichen Rückenmarkes. Mitteil. a. d. Grenzgebieten d. Medizin n. d. Chlrurgie, 1898, Bd. I. xxv. p. 415

<sup>&</sup>lt;sup>2</sup> Die Rückenmarksnerven und ihre Segmentbezuge, Berlin, 1900, Tafel i.

<sup>3</sup> Local American as a Guide in the Diagnosis of Lesions of the Lower Spinal Cord. The American Journal of the Medical Sciences, 1892, vol. elv. p. 15.

follows the distribution of peripheral nerves, and later by v. Bärensprung (1863), that it was a manifestation of lesions of the posterior root ganglia, paved the way for subsequent observations, which have culminated in the valuable studies of Henry Head on the cutaneous distribution of zoster. Head, by tabulating and plotting a large number (412) of these cases, was enabled to make a diagram of segmental cutaneous areas for almost the entire body, which in many ways proved corroborative of the facts determined by a study of cord lesions. His demonstration, furthermore, that the eruption in zoster corresponded with the areas of referred cutaneous pain and tenderness, associated with visceral disease, led him to the important conclusion that the fields which were delineated by zoster represented segmental cord areas rather than the less definitely outlined fields presided over by the individual roots. In the region, however, with which this paper deals, his chart is very incomplete from insufficiency in the number of the rarer cases of zoster which occur in the lower sacral segments. This may, in part, account for the obscure topography which his well-known figures give for the lowermost zones, where, to the uninitiated, all semblance of any segmental characteristic has been lost. This was especially true for this earlier diagram (1893), which is the one most widely copied, and, although the later one (1900)<sup>1</sup> is more satisfactory, it still remains somewhat confusing. The scheme of the sacral areas in this latter diagram is reproduced here (Fig. 9), and it will be seen that his third and fourth sacrals more nearly correspond with these territories as figured by others than they did in his original scheme.

Unless I have overlooked it, there is no mention in his classical papers in Brain of zoster occurring in or limited to the fourth and fifth sacrals and eoccygeal areas. In his first communication, there is cited as a great rarity a case from the original article of v. Bärensprung, which would appear to indicate an involvement of the lower sacral areas. There, unfortunately, is some confusion in the context, for, in describing this case, it reads "the eruption almost exactly corresponds with the two upper sacral areas." This may possibly have been a slip for the "two middle," for, although v. Bärensprung does not especially state his opinion, nor at the time of this, his first paper, had there been definite proof of the relationship of zoster to lesions of the posterior root ganglia, nevertheless, he leads one to believe, from his description of the course of the N. pudendus, which supplies this area in large part, that it arises from the three middle sacral nerves. Also, the third and fourth sacral

<sup>&</sup>lt;sup>1</sup> Head and Campbell. The Pathology of Herpes Zoster and its Bearing on Sensory Localization, Bmin, 1900, part iii., p. 353, plate 17.

<sup>&</sup>lt;sup>2</sup> Henry Head. On Distribution of Sensation, with Especial Reference to the Pain of Visceral Disease, Brain, 1893, part i., vol. xivi. p. 1.

Die Gurtelkrankheit. Armalen des Charite-Krankenbauses zn Berlin, 1861, Bd. ix. p. 100.
 Vierundfumfzigster Fall.
 Italies mine.

would more nearly correspond with the territorics which Head himself figures in his last diagram. Mackenzie¹ regards this, as well as another of v. Bärensprung's² cases, as probably indicating the distribution of the fourth sacral. Personally, inasmuch as the eruption included the præputium clitoridis, vulva, perineum, and buttock, extending slightly on to the leg, I would think that the third sacral was also included, for if there is one segmental area regarding whose representation most writers are in accord, it is the third sacral, which closely corresponds with the herpetic field in this oft-quoted case. (See the area of the third sacral in Fig. 10.)

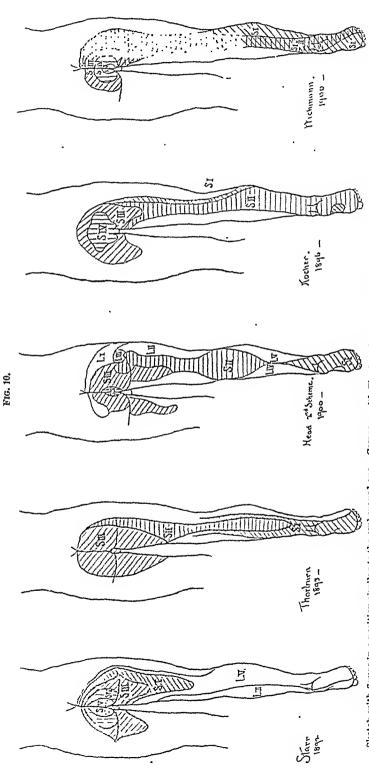
It is, of course, to be borne in mind that a herpetic eruption may only appear in patches, or maximal points, over the skin in the cutaneous zone corresponding to the involved posterior root ganglia, and, indeed, only a very small crop may be present, whereas the segment may have a broad area of representation. Furthermore, more than one segment in this situation is apt to be affected at a time which adds greatly to the difficulty of accurate demarcation of the individual ones. In the first of the cases above reported, as I have already stated, there was presumably an involvement of the ganglia from the second to the fourth sacral, inclusive, although the lesion in the latter alone sufficed to call out a herpetic rash over its own cutaneous territory.

By the "referred pain" method, Head was unable to give illustrations which would show the separate sacral areas. He calls attention to the fact, saying "that the areas making up the tract of skin over the perincum, scrotum, and penis, a portion of the buttocks, and posterior aspect of the thigh, calf and sole of the foot appear with decreasing frequency from above downward, and that if one of the lower ones is involved, it is practically always accompanied by one of the areas above it." The referred tenderness of painful bladder lesions is apt to be localized in this territory under discussion, and one of the cases which he records presented an area of cutaneous hyperæsthesia, which involved the zones probably represented by the third, fourth, and fifth sacral together. It is not at all improbable that areas of referred tenderness, or even of zoster in the sacral regions lower than the third, may, for obvious reasons, have been overlooked or unrecorded.

According to the theory originally promulgated by Ross, the limbs in their outgrowth from the trunk carry with them and distort the simple, ring-like, eutaneous units corresponding to those miatomes which enter into the limb construction. The lower four segments, lying caudalward from the hind limbs, build, just as do the dorsal nerves, more or less complete circular and concentric zones. These serially diminish in size until they reach the tip of the coccyx, which,

<sup>&</sup>lt;sup>1</sup> Herpes Zoster and the Limb Plexuses of Nerves, Journal of Pathology and Bacteriology, 1893, vol. i. p. 332.

<sup>2</sup> Loc. cit., p. 99. Dreiundfunfzigster l'all.



Sketch with figure in a position similar to the embryonal onc. Compare with Fig. 8. The zones encircle one another in serial fashion by distinct concentric strips until the IId. sacral is reached. This nerve enters entirely into a leg distribution.

of eourse, whether in embryo or adult, represents the terminal point of the human body.

Fig. 8 perhaps will elucidate this more clearly than a description. The third and fourth saeral, as indicated in the figure, are distributed in their midventral portion to the rudiments of the genitalia

surrounding the eloaea.

This distribution presumably holds true when the segments are projected on the rounded end of the adult body. In the two eases which I have reported, the fact that most of the territory involved (in Case I. by zoster, in Case II. by an area of hyperæsthesia) was in a position which in the enstomary diagrams is coneealed, has led me to make a figure (Fig. 10) which shows the nether pole of the body with the legs somewhat in the position which they occupied in the early conbryo. In the diagrams, such as are shown in Fig. 9, the upright position, eausing, as it does, a deep gluteal fold, with a hidden perineum and scrotum, makes, even in Starr's excellent scheme, the zonal distribution for these lower sagral areas somewhat obscure.

I cannot, of course, pretend to any great accuracy in the outline of these areas, believing only that the figure makes the eutaneous strips of these lower segments more intelligible than do the older diagrams, and also that for purposes of elinical utility a margin of error is preferable to a certainty of confusion. I have taken, as the average form, the fourth saeral as supplying the perineum and lower part of the serotum, the third saeral the upper part of the scrotum and penis, or corresponding organs in the female, and beginning to extend slightly down the back of the leg. It is not until we reach the second sacral, which has a leg distribution in its entirety, that we find any great degree of distortion to have resulted from the outgrowing extremities.

# ON THE LATE EFFECTS OF TYPHOID FEVER ON THE HEART AND VESSELS.

A CLINICAL STUDY.

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THE series of observations here recorded is part of a study of the eardiae and vascular complications and sequels of the eases of typhoid fever treated in the last fourteen years in the elinie of Professor Osler, at the Johns Hopkins Hospital. Though not yet as eomplete as might be desired, the material already gathered seemed

to me to be sufficient to justify an analysis of the results so far obtained.1

\* \*

The infrequency of endocarditis as a complication of typhoid fever is generally recognized. Only 11 cases were noted among the 2000 Munich necropsies, while but 3 have been observed in nearly 100 necropsies at the Johns Hopkins Hospital.

The grave myocardial changes which may occur during the disease are well known, thanks to the studies of a large number of observers, from Laennee, Louis, and Stokes, whose observations relate only to the gross appearances, down to the more minute histological investigations of Stein, Renker, Hayem, Dejerine, Romberg, Landouzy and Siredey, Renant, Mollard and Regaud, Giaeomelli, and many others. The extent of their clinical significance and their relation to the cardio-vascular manifestations of typhoid fever are still, however, questions of dispute. That the cardiae lesions as such may account for sudden collapse and death is scarcely to be doubted, but the clinical discrimination between the collapse due to disease of the heart muscle and that in which the condition is rather one of vaso-motor paralysis is often a difficult and uncertain matter. The interesting studies of Pässler and Rolly would tend to support the idea that the latter mechanism may ac-

<sup>1</sup> Read before the New York Academy of Medicine, October 20, 1903.

Traité de l'auscullation, etc., Paris, 1819, 8°, vol. il. pp. 286 et seq.

<sup>3</sup> Anatomical, Pathological, and Therapeutic Researches upon the Disease known under the Name of Gastroentérite, etc. Translated from the original French by 11. I. Bowditch, Boston, 1836, 89, vol. 1. pp. 282 et seq.

<sup>4</sup> Diseases of the Heart and the Aorta, Philadelphia, 1854, pp. 366 et seq.

<sup>4</sup> Uniersuchungen über die Myocarditis, München, 1861, 8°, J. J. Lentner, p. 115.

Deber die Veränderungen der willkürlichen Muskeln in Typhus abdominalis, fol. Leipzig,
 Vogel, 1864, pp. 29 et seq.

<sup>7</sup> Recherches sur les rapports existant entre la mort subile et les aitérations vasculaires du coeur dans la fièvre typhoïde, Arch. de phys., 1869, vol. ii. p. 698. Des compileations cardiaques de la fièvre typhoïde, Gaz. hébd. de méd., Paris, 1874, 25, vol. xi. pp. 796, 815.

<sup>8</sup> Sur les alérations du myocarde (désintegration granuleuse) comme cause de la mort subite dans la fièvre typhoïde, Compt. reud. de la Soc. de biol., 1885, 8s., vol. ii. p. 769

Ceber die Erkrankungen des Herzmuskels bei Typhus abdominalis, Scharlach und Diphtherie, Deutsch. Arch. f. klin. Med., 1891, vol. xivili. p. 369; 1892, vol. xiix, 413.

<sup>1</sup>º Contribution à l'histoire de l'artérite typhoïdique; de ses conséquences hatives (mortsubite) et tardives (myocardite selérense) du cocur, Rev. de méd., Paris, 1885, vol. v. p. 843. Landouzy, La fièvre typhoïde dans ses rapports avec l'appareil vasculaire et cardiaque, Gaz. d. hôp., Paris, 1886, vol. lix. p. 323. Landouzy et Sinedey, Étude sur les localizations anglocardiaques typhoïdiques, leurs conséquences immediates, prochaines et éloignées, Rev. de méd., Paris, 1887, vol. vil. pp. 804, 919,

<sup>&</sup>lt;sup>11</sup> Les myocardites aiguës, Congrès Français de médecine—V. session, Lilie, 1899; Paris, 1899, t. il. pp. 1-83.

<sup>&</sup>lt;sup>12</sup> État des artères du coeur dans les myocardites aiguës, Congrès Français de méd., 1899, vol. v. p. 280. Mollann, Les troubles cardiaques dans la convaiescence de la fièvre typhoïde, Presse méd., Paris, 1900, vol. i. pp. 19-22.

<sup>15</sup> Il miocardio nelle infezioni, intossicazioni, avvelenamenti. Ricerche anatomo-patologiche e sperimentali, Policiinico, Roma, 1901, viii., M., pp. 145-155.

<sup>&</sup>lt;sup>14</sup> Experimentelle Untersuchungen fiber Kreislaufstörungen bei aeuten Infectionskrankhelten, Deutsch. Arch. f. klin. Med., 1903, vol. IxxvII. p. 1.

count for more instances of eollapse in acute disease than has gen-

erally been supposed.

The part played by infectious processes in the ætiology of acute and chronic changes in the vessels is also a point toward which considerable attention has been directed in recent years.

The relative frequency of venous thrombosis in typhoid fever is familiar enough, and the probability that this is, in many instances, associated with a phlebitis depending upon local infection would seem to result from various studies of recent years.

The not infrequent arterial thromboses and acute arteritides, notably of the vessels of the extremities and of the brain, which have been studied particularly by French observers, need not be recalled. Potain has called attention to the occurrence of acute acritis.

The influence of infectious diseases in general on the production of the more insidious endarteritic changes in the aorta and other vessels—in other words, the relation of acute infections to the development of atheroma of the aorta and arterio-sclerosis in generalis a question of great importance, to which, it seems to me, we have scarcely directed sufficient attention. Numerous observers have noted the frequency of fresh gelatinous and fatty sclerotic plaques in the aorta and larger vessels in individuals dead of various acute infectious diseases, while Gilbert and Lion, 2 Crocq, 3 and others have produced sclero-calcareous and fatty sclerotic changes in the aorta of rabbits by the injection of pathogenic bacteria after previously inflicting slight mechanical injury to the walls. Indeed, Gilbert and Lion have, in several instances, succeeded in producing changes which they believe to be closely analogous to those observed in human arterio-sclerosis by the intravascular injection of pathogenic organisms without the previous production of a point of least resistance by injury. On the other hand, Thomas mentions typhoid fever among the ætiological elements in the production of that angiomalacia which he believes to be the primary lesion in the development of arterio-sclerosis.

In brief, there is much which goes to suggest that acute infections, and typhoid fever among them, play an important part in the ætiology of arterio-selerosis. Some observers who have especially studied this question believe that after acute rheumatism typhoid fever is the infectious disease most frequently resulting in changes in the heart and vessels.

<sup>&</sup>lt;sup>1</sup> De l'aortite typhique, Semaine méd., Paris, 1894, vol. xiv. p. 460.

<sup>&</sup>lt;sup>2</sup> Artérites Infectieuses expérimentales, Comptes rend. de la Soc. de biol., Paris, 1889, 9s., vol. i. p. 583.

<sup>\*</sup> Contribution à l'étude expérimentale des artérites infectionses (abstr.), Arch. de méd. exp. et d'anat. path., Paris, 1891, vol. vi. pp. 583-600.

Ueber das elastiehe Gewebe der Arterlenwand und die Angiomalaeie, Verhandlungen des XIII. Cong. f. inn. Med., Wiesbaden, 1895. p. 465.

The observations of Landouzy and Siredey¹ are especially striking. These authors report the case of a man, aged twenty-three years, who died suddenly on the fifteenth day of typhoid fever. Two years before he had passed through a serious typhoid infection of six weeks' duration. The heart musele showed extensive acute inflammatory and degenerative changes in association with grave older selerotie alterations. There was nothing in the history of the patient, beyond his previous typhoid fever, to which these alterations eould be ascribed. Out of 15 typhoid patients between five and forty-eight years of age, followed by Landouzy for a period of nine years, there were 3 in whom marked eardiae disturbance had persisted after recovery from the acute disease. These 3 patients, five, three, and two years after the disease, all showed a certain degree of hypertrophy, with eardiac irritability. As a result of their study, Landouzy and Siredey maintain among their eonclusions that: "The secondary angio-eardiac complications of typhoid fever are more frequent than is generally believed and than has been generally acknowledged up to the present time.

"After acute articular rheumatism, typhoid fever appears to give rise to more angio-eardiae complications than any of the other infec-

tions diseases.

"Among the most important and commonest of these complications are those which arise insidiously during the course or decline of the The angio-cardiae lesions are important to reeognize, less because of the prognostic reserve which they demand during the eourse of the disease itself (collapse, sudden death) than for that which they impose upon us for the future."

And Lacombe,2 among the conclusions of his thesis, maintains that: "The disorders of the heart appearing some years after recovery from typhoid fever may be legitimately ascribed to this disease, if no other malady capable of compromising the integrity of the heart, either before or after the typhoid, has occurred."

The communications of Landouzy and Siredey especially suggested to me that it might be of interest to make a series of observations as to the condition of the heart and vessels in a number of individuals who had had typhoid fever in the wards of the Johns Hopkins Hospital during the past fourteen years, comparing these results with the previous hospital records, which, in many instances, are fairly complete. This proceeding appealed to me the more because, so far as I know, it has never been previously attempted. With this end in view, I sent out letters to all patients who had had typhoid fever in the wards of the hospital since its opening in 1889—over 1400 in all. In the majority of instances, as might have been expected, the letters failed to reach their destination and were returned, but 183 patients presented themselves for examination.

<sup>1</sup> Op. cit., 1885. <sup>2</sup> Localizations angiocardiaques de la fièvre typhoide, Paris, 1890, 4°.

The majority of these patients were examined at the hospital between 3 and 5 o'clock on Sunday afternoons. About 30 per cent. of the cases were studied in the Out-patient Department between the hours of 10 and 12 in the morning. The measurements of the heart, the record of the pulse, and the estimations of the blood pressure were made in the recumbent posture for comparison with the hospital records.

AGE AND DATE OF ATTACK.

The ages of the patients varied between three and sixty-nine years, while the periods which had elapsed between the discharge from the hospital and the subsequent examination ranged from one month to thirteen years. In all cases the patient was questioned as to the maladies from which he might have suffered since his discharge from the hospital. The following table will show the period of time which had elapsed between the discharge from the hospital and the subsequent examination of the patients:

TABLE I.

Showing the length of time which had clapsed between the discharge of the patient from the hospital and his subsequent examination.

	iths.							Year	3.					
	6-12	1	2	3	4	5	6	7	8	9	10	11	12	13
22	26	18	20	23	21	11	13	11	8	6	2	0	1	1 = 182

Pulse.

(a) Rate. Most of the patients at the time of their examination had already rested for some little period of time after their arrival at the hospital. In a large proportion of the eases, however, there was a manifest nervousness; no more, probably, than is eommon on the examination of any one under similar eireumstanees; perhaps a trifle less, inasmuch as the patients were for the most part old friends.

The following table shows the rate of the pulse in 182 eases:

### TABLE II.

Rate of the pulse per minute.

50-60	60-70	70-S0	80-90	90-100	100-110	110-120	120-130	Not noted.	Totai.
1	17	42	50	26	23	8	8	17	182

In this table it will be seen that in 110 instances, or 60.4 per cent. of the eases, the pulse ranged between 60 and 90. In 16 instances, or 8.7 per cent., it was above 110.

(b) Regularity. In 30 instances irregularity of the pulse was noted;

four of these were eases in which the rate was not recorded.

Of the eases in which the pulse was over 90, irregularity was noted in 18.3 per cent.

Of the eases in which the pulse was under 90, irregularity was observed in 12.7 per cent.

(c) Intermittence. In only 3 instances was the pulse distinctly intermittent. One of these was a well-marked case of hypertrophy

<sup>1</sup> There were but three eases seen under three months from the time of discharge.

with mitral insufficiency. There were 2 eases in which a strikingly collapsing character of the pulse was noted. In each of these instances an aortic diastolic murmur was present.

BLOOD PRESSURE.

In 165 of these eases the systolic blood pressure was taken by means of the Riva-Rocei apparatus. This proceeding was made the last step in the examination, in order that the patient might be in as placid a condition as possible. The estimations were repeated several times until constant readings were obtained. The band was always placed around the middle of the upper arm, right or left.

The results of these estimations are indicated in the following table:

TABLE III.

Showing the averages of the systolic blood pressure in 165 old typhoids arranged by age according to decades.

1-10	10-20	20-30	30-10	40-50	50-60	60-70
112.4 mm.	135.2 mm.	153.5 mm.	161.5 mm.	170 2 mm.	179.6 mm.	215 mm.
(5 cases )	(39 cases )	(58 cases )	(14 cases.)	(15 eases.)	(3 cases.)	(1 case.)

Struck by the high averages of the systolic blood pressure in this group of eases, I sought for statistics with which these figures might be compared, but soon found that it would be necessary, in order to reach a fair conclusion, to make myself a series of observations upon normal individuals under conditions as similar as might be. I have, therefore, in the last several months made 276 estimations of the blood pressure in presumably healthy individuals. These observations were made upon physicians, nurses, and employes of the hospitals, friends of patients, healthy children in several different asylums and schools, and upon various of my own friends. I did not allow myself to record the blood pressure of any patient, surgical or medical, no matter what his complaint. The records were taken between the hours of 3 and 5 in the afternoon or between 10 A.M. and 1 P.M.; in other words, several hours after a meal. They were all taken in the recumbent posture, sufficient time being taken to allow the individual to recover from the preliminary nervousness; that is, under conditions similar to those employed in making the observations upon the previous group of patients. The averages of this table, which may be seen upon Chart I., show a distinctly and uniformly lower blood pressure than in the old typhoids.

TABLE IV.

Showing the averages of the systolic blood pressure in 276 healthy Individuals and 165 old typhoids arranged according to age by decades.

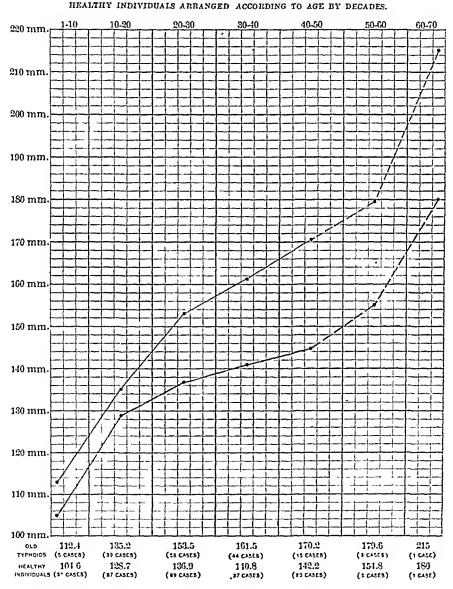
			Ola typnolas.	•		
1-10	10-20	20-30	30-10	40~50	50-60	60-70
1124 mm.	135 2 mm.	153 5 mm.	161.5 mm.	170.2 mm,	179.6 mm.	215 mm.
(5 cases.)	(39 cases.)	(58 cases.)	(44 cases )	(15 cases.)	(3 cases.)	(1 case.)
		Her	thiribai vatt	ายไร.		

		nea	ning marriad	1612*		
104.6 mm.	1287 mm.	136.9 mm.	140 8 mm.	142.2 mm.	154 8 mm.	180 mm
(37 cases.)	(S7 cases.)	(89 cases.)	(37 cases.)	(20 cases.)	(5 cases.)	(I case.)

Inasmuch as all observers agree that the average blood pressure is slightly lower in women than in men, it may be well to note that the proportion of women was higher among the old typhoids than among the eases from which the control table was constructed, the exact figures being 38.7 per cent. for the old typhoids and 33.3 per cent. for the normal cases.

CHART I.

SHOWING AVERAGES OF THE SYSTOLIC BLOOD PRESSURE IN 165 OLD TYPHOIDS AND IN 276



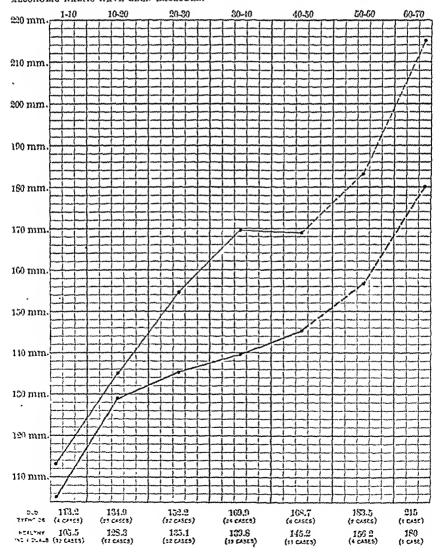
On the other hand, more of the normal cases were examined during the morning hours than of the old typhoids, the percentage being 40.5 per cent. to 30.3 per cent.

A closer analysis of the figures upon which these tables are based reveals the fact that among the old typhoids there were 54 cases in which the blood pressure was above 160; this group comprises over 50 per cent. of the cases over thirty years of age.

In the much larger number of observations upon healthy individuals there were but 10 such cases, 6 of which gave a history of preceding serious infectious disease, while in 1 there was a good suspicion of alcoholism. Of the 54 old typhoids, in but 17 was a similar history obtainable.

#### CHART II.

SHOWING THE AVERAGES OF THE SYSTOLIC BLOOD PRESSURE IN OLD TYPHOIDS AND IN NORMAL INDIVIDUALS FROM WHOM ALL CASES WITH A HISTORY OF SERIOUS INFECTIOUS DISEASE OR ALCOHOLIC HABITS HAVE BEEN EXCLUDED.



The highest record of blood pressure among the cases in healthy individuals was 180, and that in a woman aged sixty years, while among the old typhoids there were 27 cases in which the pressure was above 180, a number of which were striking examples of hypertension, 10 showing a record of 200 or above.

It might be objected that to ascribe this difference between the two curves to changes dependent upon the preceding typhoid fever would be a rash conclusion, inasmuch as a great number of other influences must have eome into play, while the number of cases studied is too small to justify positive conclusions. In order to rule out some of these disturbing influences, I have prepared a table in which I have eliminated from each list all those cases in which a history of scarlet fever, diphtheria, acute rheumatism, pneumonia, erysipelas, smallpox, syphilis or alcoholic habits could be obtained. This table, which is represented graphically on Chart II., shows essentially the same relation between the two curves:

# TABLE V.

Showing the averages of the blood pressure in old typhoids and normal individuals, from which all cases with a history of serious infectious disease or alcoholic habits have been excluded.

Old typhoids.

1-10 113.2 mm.	10-20 131.9 mm.	20-30 152.2 mm	30–40 169.9 mm.	40-50 168.7 mm.	50-60 183.5 mm.	60-70 215 mm.				
(4 cases)	(28 cases.)	(32 cases)	(21 cases)	(8 cases.)	(2 cases.)	(1 case.)				
	Healthy individuals.									
105.5 mm.	128.3 mm.	135.1 mm.	139.8 ınm,	145.2 mm.	156.4 mm.	180 mm.				
(32 cases.)	(62 cases)	(52 cases.)	(19 cases.)	(11 cases.)	(4 cases.)	(1 case )				

The average of the observations upon healthy individuals is about 2 mm. less than in the uncorrected list. That of the typhoid observations is practically unchanged. The alteration in the typhoid curve on the chart arranged by decades, due to the higher figures in the 30–40 column, emphasizes the fact that the number of cases is still too small to allow of the construction of final charts.

# PALPABILITY OF THE RADIAL ARTERIES.

Note was also made of the palpability of the radial arteries. In order to obviate the common confusion arising from a full vessel or engorgement of the venæ comitantes, the blood was milked out of the artery and veins with the fingers of both hands, the tense tissues relaxed, while with a third finger an attempt was made to feel the empty vessel. The following table will show the results of observations on 181 old typhoids:

Showing the palpability of the radial arteries in 181 cases arranged by age according

		n 15] CR565 F	III I I I I I I I I I I I I I I I I I	•
ing the palpability of the	radial arteries i to decade	S 330	Palpable.	Per cent. of palpable vessels.
mg	Cuzes. Zot.	-	0	25.5
Age.	. 5	30	12 33	53.2
1-10	. 42 62	29	20	53.7 50
10-20 20-30	. 54 . 54	25 7	7	100
30-40	. 11	0	9	0
40-50 50-60	, .3 1	1	•	that over 50
60-70	·	the stri	king <sup>fac</sup>	t that over 50 ed palpable ra
	-ac reveille	,	"I'Otlo	eu vuni 🔒 🕕

A glance at these figures reveals the striking fact that over 50 per A game at these ngures reveals the striking fact that over 50 percent. of our cases above twenty years of age showed palpable radial cent. of our cases above twenty have the radials were not palpable, I the arteries. In 2 instances in which the radials were not palpable, I the

SHOWING THE PERCENTAGES OF PALPABILITY OF THE RADIAL ARTERIES IN OLD TYPHOIDS AND

rteries.	THE PERCENTAGES IN HEALTHY IND		or III.		S OLD TYPHO!	DS AND	
11022	THE PERCENTAGES IN HEALTHY IND	GH	THE RADI	AL ARTERIES I	DECADES.		
		or palpability	OF THE ACCORDIN	G TO AGE BY	20.60	60-70	
	HE PERCENTAGES	TINTIALS ARRA	ZGED Zee	40-50		T-1-1-1	
SHOWING T	IN HEALTHY IND	14100-	30-10		1-1-1	1-1-1	
	10-20	20-30	TIH			1111	
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		1-17-1-1				+++++	+1
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			11-1-1	工十十二	17-1-1		
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	HEYTANG (SE EYEES	7 (4.0					

ease of a man aged twenty-five years, and 1 that of a woman aged forty-seven years, one or the other of the temporal arteries was distinctly thickened. In general, I have in these studies been impressed with the irregularity in the distribution of the selerotic processes in peripheral vessels. It is by no means uncommon to find one radial or temporal distinctly thickened or tortuous, while the other is apparently unaffected.

A comparison of the observations recorded in this table with those made upon the patients while in the hospital is of little value, in view of the fact that a definite note as to the palpability of the radials was made in but 48 eases. These figures, which were even more striking than the high averages of blood pressure, could, it seemed to me, be fairly compared only with a similar series of observations made by myself upon supposedly healthy individuals who had not suffered from typhoid fever. Within the last several months, accordingly, I have examined the radials and temporals of 421 individuals who have never had typhoid fever. The accompanying table, illustrated on Chart III., shows a comparison of the percentages of palpable radials arranged by decades in our old typhoids and in healthy individuals:

TABLE VII.

Showing the percentages of palpability of the radial arteries in old typhoids and lu healthy individuals arranged according to age by decades.

			Old typhoids.	•		
1–10 0 %	10-20 28.5 %	20-30 53.2 4	30 <b>-4</b> 0 53.7 ≰	10-50 50 %	50-60 100 ಕ	60-70 0 ਵ
(5 cases.)	(42 eases.)	(62 enses.)	(54 cases.)	(14 cases.)	(3 cases.)	(1 case.)
		He	althy individi	ials.		
0 % (37 eases.)	6.1 % (98 eases.)	20.4 % (86 cases.)	25 % (61 cases.)	22 (r (27 cases.)	42.8 \$ (7 cases.)	80 ¢ (5 cases.)

By these figures it appears that between the ages of ten and fifty years 46.8 per eent. of the old typhoids showed palpable vessels as compared with 17.6 per eent. of the normal cases.

I have also prepared comparative tables, as in the ease of the records of blood pressure, based upon an analysis of those eases only in which a history of serious infections or of habits which might induce arterio-selerosis was wanting. This table is illustrated by Chart IV.

## TABLE VIII.

Showing the percentages of palpability of the radial arteries in old typhoids and in healthy individuals from which all cases giving a history of serious infections or alcoholism have been excluded.

			Old typhoids.	•		
1-10	10-20	20-30	30-40	40-50	50-60	60-70
0 ;	22.5 %	51.2 f	62.9 ¢	57.1 %	100 \$	0 %
(4 cases.)	(31 cases.)	(35 eases.)	(27 cases.)	(7 cases.)	(2 enses.)	(1 case.)
		11e	ılthy indlyldı	ials.		
0 %	4.2 ½	21.3 ¢	22.2 \$	18.7 #	33.3 %	75 ¢
(32 cases.)	(70 cases.)	(103 cases.)	(27 cases.)	(16 cases.)	(6 cases.)	(4 cases.)

As in the ease of the observations upon the blood pressure, the total average is slightly lower among the healthy individuals—15.1 per cent.: 17.5 per cent. Among the typhoids the average palpability of the vessels in this list varies but little from that in the previous table—45.7 per cent.: 46.1 per cent.

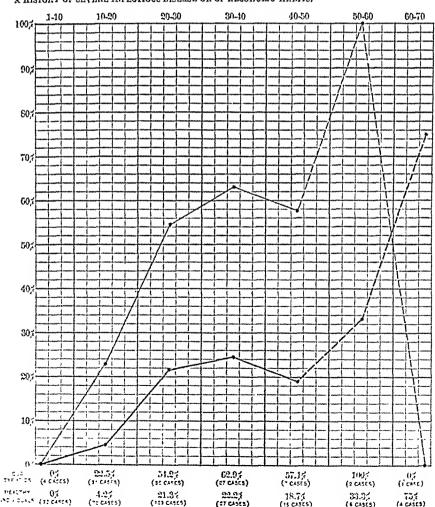
HEART.

Position of the Apex. Measurements of the distance of the apex of the heart from the median line were made in 180 of the old typhoids. The average distance of the apex from the median line as determined by palpation, percussion, and auscultation in individuals between the ages of twenty and fifty years was 9.12 cm.

· Similar measurements made in 102 of these cases on admission to the hospital showed an average of 8.7 per cent.

CHART IV.

SHOWING THE PERCENTAGES OF PALPABILITY OF THE RADIAL ARTERIES IN OLD TYPHOIDS AND IN HEALTHY INDIVIDUALS AFTER THE REMOVAL FROM EACH LIST ALL CASES IN WHICH THERE IS A HISTORY OF SEVERE INFECTIOUS DISEASE OR OF ALCOHOLIC HABITS.



The following table shows the averages, arranged according to age by decades, of 102 cases which were examined on admission to the hospital, side by side with the records of those examined later:

TABLE IX.

Showing the average distance of the cardiac apex from the median line in 102 cases of typhoid fever on admission to the hospital, and of 180 cases examined later.

			Old typhoids	i.		
1-10 6.3 cm. (5 cases.)	10-20 7.7 cm. (41 eases.)	20-30 8 9 cm. (63 eases.)	30–40 9.1 cm. (52 cases.)	40-50 9.8 cm. (15 cases.)	50-60 9.5 cm. (3 cases.)	60-70 12 cm. (1 case.)
			During attack	٤,		
5.7 cm, (5 cases.)	6.6 cm. (36 cases.)	8,5 cm. (38 eases.)	8.5 cm. (14 cases.)	9.6 cm. (9 cases.)		

It will be noted that the average measurements in the old typhoids are slightly but constantly larger than in the cases examined on admission to the hospital. Though this difference, as shown by the table, is trivial, it should, perhaps, be borne in mind that there is not infrequently in typhoid fever a slight dilatation of the heart, and that most of these examinations were made when the fever was well under way.

Inasmuch as 46 of these cases entered the hospital when they were under twenty years of age, that is, at a time when, in many instances, they had not attained full development, it seemed wise to investigate the position of the apex in individuals over twenty years at the time of their admission, where notes had been made both in the hospital and subsequently. There were 59 such cases. At the time of admission the average distance of the apex from the median line was 8.82 cm.; subsequently it was 9.14 per cent., a slight difference, but one which corresponds closely with the larger averages.

Extent of the Cardiac Dulness to the Right. In 158 eases examined by myself a note was made as to the extent of the cardiae dulness to the right of the midsternal line. The average distance for each decade is shown in the following table:

#### TABLE X.

Showing the average extent of the cardiac dulness to the right of the midsternal line in 158 old typhoids arranged according to age by decades.

1-10	10-20	20-30	30-10	-1050	50-60	60-70	
2.4 cm.	3.12 cm.	3.45 cm.	3.39 cm.	3.47 cm.	3.4 cm.	5 cm.	
(3 cases.)	(36 cases.)	(54 cases.)	(47 cases.)	(14 cases.)	(3 cases.)	(1 case.)	

The greatest extent of dulness to the right of the median line among these cases was 5 cm., in a man with dilated heart and mitral insufficiency.

In but 1 case, that of a man aged thirty years, was no dulness to the right to be made out. This case accounts in great part for the slightly lower average in the fourth decade. There is nothing remarkable about these figures, which are, indeed, a trifle smaller than those given by Riess.<sup>1</sup>

Heart Sounds, In the Hospital. In 170 of these cases in which notes with regard to the condition of the heart sounds were made in the hospital, murmurs were noted in 39 instances, or 29 per cent. In 31 cases the murmur was a soft systolic blow heard at the apex, and only once was the sound transmitted to the axilla. In a number of cases this murmur was heard only on admission or at the height of the disease, disappearing with convalescence. In 5 of these 31 cases the pulse in the hospital was above 140, one case, however, being under fifteen years of age.

On Later Examination. Notes on the heart sounds were made in all but 2 of the 183 old typhoids. 88, or 48.6 per cent., of these cases showed murmurs. In all of these the murmurs were systolic, although in 2 instances an aortic diastolic murmur was heard in

addition, and in one case a doubtful mitral presystolic.

In only 38 cases was the systolic murmur audible at the apex. In the majority the murmur was a soft blow, with its maximum intensity at the base of the heart, in the pulmonic or nortic area.

In 11 cases an apex systolic murmur was transmitted to the axilla, and in 7 was audible also in the back. In 7 cases the symptoms justified the diagnosis of mitral insufficiency (Nos. 9921, 10,704, 10,714, 31,173, 17,636, 28,249, 36,210). One further case (20,507), an instance of aortic insufficiency, showed also evidences of mitral incompetency. In one case (32,037) there were signs suggesting mitral stenosis.

In 2 instances aortic diastolic murmurs were heard in cases which had previously shown no evidence of cardiac trouble (39,371, 26,507). One of these individuals, who was examined nearly four months after discharge from the hospital, was seen again five months later, at which time the diastolic murmur had entirely disappeared and the size of the heart had slightly diminished. This case must probably be regarded as one of functional insufficiency, due to relaxation

of the aortic ring.

Reduplication of the First Sound. In 14 of the old typhoids a reduplication of the first sound at the apex or trienspid area was observed. One of these was a case of well marked hypertrophy, with mitral insufficiency; another was a case of Graves' disease, with high arterial tension. In general, it was noted that the arterial tension in cases showing reduplication of the first sound was high, the average pressure being 164.9. In 3 cases the pressure was above 200. In only one of these reduplications did it seem possible to determine the cause of the split in the first sound. In this case it was clearly due to delay in the closure of the tricuspid valve.

<sup>&</sup>lt;sup>1</sup> Sahli. Lehrbuch der klinischen Untersuchungsmethoden, Lelpzig u. Wien, S Auflage, 1901, <sup>49</sup>, p. 165.

Reduplication of the Second Sound. In 82 of the old typhoids there was a reduplication of the second sound. This, in every instance but one, was audible at the base and usually limited to the pulmonic area. In 73 cases the reduplication was clearly dependent upon delay in the closure of the pulmonic valves. The reduplications were usually slight and heard only at the end of inspiration—cases such as would fall into Galli's¹ class of "reduplications of the first grade." In 10 cases, however, the reduplication was heard throughout the entire cycle.

The proportion of reduplications is not far from that observed by Galli, who, in his 120 carbineers, found 19 per cent. of such reduplications in the morning, 40 per cent. at noon, 56 per cent. in the afternoon

The blood pressure of these eases was slightly below the general average for the old typhoids of the same decades—148.3:152.

Accentuation of the Second Sound. Out of 161 cases in which the relative accentuation of the aortic or pulmonic second sounds was noted, the pulmonic second was accentuated in 82, or 50.9 per cent. The following table will show the relative percentages of accentuation of the second aortic sound, arranged according to decade:

1-10	10~20	20-30	30-10	40-50	50-60	60-70
20 s	30.3 %	48.2 ಡ	44.6 4	46.6 %	100 ಳ	100 ≴
(5 cases.)	(33 cases.)	(58 cases.)	(47 cases.)	(15 cases.)	(2 cases.)	(1 casc.)

Compared with the figures of Cabot, the percentages in the lower decades are high, while those above the third decade are low. I do not, however, attach any great importance to these figures. In using the term "accentuated" I have intended to indicate that sound which was actually the louder of the two. In a number of instances, however, the second aortic sound, while not apparently as loud as the second pulmonie, was ringing, liquid, musical and suggestive of high tension. Again, the study of reduplications of the second sound, among other things, proves, I think, clearly that in many instances the closure of the aortic valve plays the greater part in the production of the loud sound which one hears in the pulmonic area.

SUMMARY OF THE GENERAL ANALYSES.

To summarize the results of these general analyses we have found:

1. That our old typhoids show an average blood pressure higher than that observed in control tables of normal subjects of the same age and under the same conditions, while the individual

Munch, med. Wochenschr., 1902, vol. xlix, pp. 95, 1005, 1049.

<sup>2</sup> Physical Diagnosis of Diseases of the Chest, 2d ed., 1903, 82, p. 121.

records in a considerable proportion of cases exceed the figures

usually regarded as normal.

2. That in these same cases the radial arteries are palpable with much greater frequency than was observed in a series of control observations in individuals who had never had the disease.

3. That there is some evidence of cardiac enlargement, as indicated by the results of measurements of the distance of the apex from the median line when compared with figures for the same decade resulting from observations made at the time of admission

to the hospital.

4. That there were among these 182 old typhoids 10 instances of cardio-vascular lesions, which had developed following typhoid fever in the absence of the ordinarily recognized ætiological elements; 7 cases of hypertrophy with mitral insufficiency (10,704, 10,714, 31,173, 17,636, 24,675, 28,249, 36,210); 1 two of aortic insufficiency (39,371, 20,507); one of marked arterio-sclerosis with hyper-tension in a young man (17,632).

In addition to these cases there was one instance of possible mitral

stenosis (32,037).

\* \*

Are the more serious cardio-vascular manifestations during typhoid fever common precursors of permanent lesions? Is it in eases presenting such symptoms that the grave, later changes develop? Is it possible to recognize at the time of their origin the development of those processes which subsequently exert a permanent effect upon the organism?

In order to obtain some light upon these questions, it was determined to examine separately into the subsequent condition of:

1. Those cases in which, during the attack, extreme rapidity of the pulse was noted.

2. Those cases where irregularity of the pulse was observed.

3. Those cases in which an apical systolic murmur was heard.

1. The Subsequent Condition of Those Cases of Typhoid

FEVER IN WHICH EXTREME RAPIDITY OF THE PULSE WAS NOTED DURING THE ATTACK.

Rate of the Pulse: In 19 cases a pulse of 140 or above was recorded during the attack. 9 of these patients were under twenty years of age at the time of admission. The rate of the pulse in the remaining 10 cases on subsequent examination shows no great variations from the general average. In 2 instances the rate was not noted. In one, a case of Graves' disease, it was 120; in one, 104; in one, 92; and in the other 5 instances, or 50 per cent., the pulse was between 68 and 84.

Systolic Blood Pressure. Of the 19 cases in which an extremely rapid pulse was observed in the hospital, 9 who were under twenty

<sup>1</sup> In one other case (9921) it is well possible that the typhoid fever may have been the exciting cause of the condition.

years of age have been omitted from the list; it is easily conceivable that in individuals under twenty years a pulse of 140 may not represent the same conditions as a pulse of that rate at a later age. Of the remaining 10 cases, varying in age from twenty-two years to fifty-three years, the average systolic pressure was 166.8. The general average of the old typhoids for these decades was 159.2. There were among these 10 cases, 2 with a blood pressure above 200, and 5, or 50 per cent., with a pressure above 160.

Palpability of the Radial Arteries. In 4, or 40 per cent. of these 10 cases, the radial artery was palpable. The general average for

these decades among the old typhoids was 53.7 per eent.

Position of the Apex of the Heart. In only 4 of the 10 cases were measurements made during the disease. The average distance of the apex from the median line in these eases was 7.37 cm. In 10 cases examined subsequently the average distance was 8.48 cm. In the 4 cases in which a hospital record was made the average distance of the apex from the median line in the later examinations was 8.5 cm. If we compare these figures with the average of the measurements on admission to the hospital—8.82—and the average for the old typhoids—9.14—we find that they are lower in both instances. The difference, however, between the measurements during the disease and later is greater in the smaller group.

Extent of the Cardiac Dulness to the Right. In none of these 10 eases were measurements of the eardiae dulness to the right made during the fever. The average extent of dulness to the right of the median line on subsequent examination was 3.61, or slightly more

than the total average for the same decades—3.44.

In review, then, we have found that in 10 eases over twenty years of age who, during their typhoid fever, showed extreme rapidity of the pulse, there was on subsequent examination, an average blood pressure somewhat higher than that observed in the mean of the whole 165 eases; the percentage of palpability of the radial arteries was less; the distance of the apex of the heart from the median line was somewhat less; while the extent of the dulness of the heart to the right of the median line was a trifle above the general average. The increase in the size of the heart during the period subsequent to the illness was somewhat above the general mean. Two eases showed distinct hypertrophy, with hyper-tension (11,331 and 14,675); in one of these there was evidence of mitral insufficiency.

2. Subsequent Condition of Those Cases in Which Irregularity of the Pulse was Noted during the Attack.

Rate and Rhythm of the Pulse. Irregularity of the heart's action was noted in 12 eases during the attack. In 1 of these the irregularity occurred in association with the bradycardia (46) of convalescence. In 2 eases irregularity was observed on the subsequent examination. In the remaining 10 nothing remarkable was noted as to rate or rhythm of the pulse.

The Systolic Blood Pressure. In 11 of these 12 cases the average blood pressure on the later examination was 152.2 mm., as compared with the general average of 152 mm. 3 cases were under fifteen years of age. If we put aside these 3 cases in which the average pressure was 113.3 mm., there are left 8 cases, aged between twenty years and forty-two years, in whom the average pressure was 166.8 mm. The average pressure among the old typhoids for these decades was 158.6 mm. In 2 instances the pressure was above 200.

Palpability of the Radial Arteries. The radial arteries were

palpable in but 3, or 27.2 per cent., of these cases.

Position of the Apex. The position of the apex was noted in the hospital in 9 of these cases. In 4, under twenty years of age, the average distance of the apex from the median line was 7.12 cm. In 5, over twenty years, the average distance was 8.2 cm. Of the 12 cases on the later examination, in 3, under twenty years of age, the average distance of the apex from the median line was 6.6 cm. In 9, over twenty years, it was 8.18 cm. In the 4 cases in which a hospital note was made the average distance of the apex from the median line on subsequent examination was 8 cm., or 0.2 cm. less than the average in the hospital.

Extent of Dulness to the Right. In none of these cases was a measurement made in the hospital of the extent of the cardiac dulness to the right. In 11 instances a record was made on the later examination. In 3 cases, under twenty years of age, the average was 3 cm. In 8 cases, over twenty years, the average was 3.35 cm. Review. In the 12 cases which in the hospital showed irregularity

of the pulse, as in the cases with rapid pulse, the blood pressure, on later examination, was found to be distinctly higher than the general mean of the 165 old typhoids. On the other hand, there was no evidence of cardiac enlargement; the distance of the apex from the median line was, indeed, less than in the general mean, or in the same cases on admission to the hospital. The percentage of palpability of radial arteries was also lower than the general average.

3. THE SUBSEQUENT CONDITION OF THOSE CASES IN WHICH AN APICAL SYSTOLIC MURMUR WAS NOTED DURING THE ATTACK.

The Rate of the Pulse. Of the 31 patients in whom during their fever a systolic murmur was observed, in 29 the rate of the pulse was noted in the subsequent examination. Twenty-one, or 72.4 per cent. of these cases, showed a pulse between 76 and 88. In 2 instances the pulse was between 90 and 100; in 5, between 100 and 110; and once only 120, a case of Graves' disease. When these figures are compared with the foregoing records for the total number of cases, it becomes evident that there is no apparent tendency in this group of cases to an increased rapidity of the pulse.

Palpability of the Radial Arteries. In 30 of these cases in which a note as to the palpability of the radial arteries was made, the vessel was to be felt in 11, or 36.6 per cent., as compared with the

general average of 46.1 per cent.

The Systolic Blood Pressure. In 28 of these 31 eases the systolic blood pressure was taken in the later examination. The average of these 28 eases was 158.5 mm., against the general average for the total number of cases of 152.4. This higher average was observed in every decade excepting the first, in which there was but I case, and the third, in which there were but 4. In 18 eases, over the age of twenty years, the average pressure was 169.2, as compared with the general average of 159.6 for the same decades. In 5 eases the pressure was 200 mm. or above.

Position of the Apex. In 22 of these eases the position of the apex was determined in the hospital, the average distance from the median line being 7.1 cm. In 30 cases a subsequent note was made, the average being 8.9 cm. The former figures arc slightly lower than the general average, the latter slightly higher. If we subtract from this list of cases those who were under twenty years at the time of admission, the average becomes 8.54 cm. in 11 hospital cases, against 9.4 cm, in 19 cases examined later. If we further compare only the 11 cases in which notes were made both in the hospital and later, the averages are, respectively, 8.54 cm. and 9.25 cm. Comparing these figures with the general hospital averages for the same decades, 8.70 and 9.22, it is evident that this small group of cases in which systolic murmurs were heard at the apex during their attacks showed, on later examination, measurements essentially the same as in the general average, despite the fact that at the onset of the disease the average for these same cases was slightly below the general mean.

Extent of Cardiac Dulness to the Right. In none of these eases was the dulness to the right measured while the patient was in the hospital. In the subsequent examinations a record was made in 29 eases, the average extent of dulness being 3.39 cm., as compared with the total average for all decades of 3.35. 9 of these patients who were under twenty years of age showed an average measurement of 3.3 cm., as against the general average of 3.08, while the 20 eases over twenty years of age showed an average measurement

of 3.43, as compared with the general average of 3.44.

Heart Sounds. In but 2 of the 31 cases in which a systolic apieal murmur was heard in the hospital was the sound transmitted to the axilla, and in neither of these instances were the signs such as might have justified a diagnosis of organic cardiae disease.

On the later examination:

In 11 instances the heart sounds were clear.

In 1 ease there was a slight eardio-respiratory murmur at the. apex.

In 6 cases there was a soft systolic murmur at the base, in some instances heard also over the right ventricle.

In 13 cases there was a systolic murmur at the apex of the heart.

Of these 13 cases:

In 5 the murmur was a soft systolic blow heard at the apex, and in 3 instances also over the rest of the cardiac area. In the 2 cases where the murmur was limited to the apex it disappeared in the erect posture.

In 5 the signs justified the diagnosis of mitral insufficiency.

In 1 there were signs suggestive of mitral stenosis.

In 1 there was marked arterio-sclerosis, with hyper-tension, and a slight systolic murmur at the apex, tricuspid, and pulmonic areas. In 1 there was Graves' disease, with a systolic murmur all over

In 1 there was Graves' disease, with a systolic murmur all over the cardiac area. This condition was present also at the time of the fever.

Review. On considering these figures, we find that the 31 cases in which systolic murnurs were observed during the fever showed, on later examination, nothing remarkable with regard to the pulse, while the palpability of the peripheral arteries was below the general

average for the old typhoids.

On the other hand, the blood pressure was strikingly higher than the general average, one-half of the cases of extreme hyper-tension (200 mm. or above) being observed in this small group. The size of the heart was also increased, as compared to the mean of our observations upon the old typhoids, while the actual increase in those cases in which measurements were made in the hospital and later was also greater than the general average.

Seven or nearly one-quarter of these cases, showed, on subsequent examination, evidence of organic cardiac lesions, while another case was a striking example of general arterio-sclerosis, with hyper-

tension, in a young individual.

\* \* \*

Among these 183 cases there are several which deserve special attention.

Case I. Hypertrophied heart; mitral insufficiency.—Mrs. H. B. (Hospital No. 9921), aged forty years, was admitted to the hospital on April 19, 1894, where she passed through a typhoid fever of thirty days' duration, complicated with neuritis of the left ulnar nerve. The urine was free from albumin. Previously she had been a healthy woman, excepting for an attack of acute articular rheumatism at six years, and three attacks since then. In the hospital records it was noted that there was no increase in the area of cardiac dulness; that the sounds were clear at the apex. The highest recorded pulse was 116.

On January 5, 1903, the patient reported for examination in answer to my letter. She had had no illness since leaving the hospital. She

had, however, complained of late of being somewhat short of breath on exertion. The pulse was 22 to the quarter, regular, of good size, rather long duration. The radial artery was just palpable; temporals

not prominent. Systolic blood pressure, 200 mm.

Heart. Point of maximum impulse in the fifth space 10 cm. from the midsternal line. Dulness extends 4 cm. to the right of the midsternal line. At the apex the first sound is replaced by a well-marked blowing systolic murmur; the second is clear. The murmur is heard distinctly throughout the axilla and in the back. It is audible also in the tricuspid, pulmonic, and aortic areas, over the manubrium, and in the carotids. The aortic second sound is sharp, though scarcely as sharp as the second pulmonic, which is accentuated. There are one or two reduplications of the second sound in the pulmonic area at the end of each inspiration, the second part of the split sound being accentuated. This reduplication is occasionally heard in the aortic area, where the accented part is clearly the first.

In this case it is possible that a valvular lesion, though not evident at the period when she was in the hospital, may have dated from her preceding attacks of rheumatism.

Case II. Moderate hypertrophy of the heart; mitral insufficiency.—E. T. E. (Hospital No. 10,704), aged twenty-five years, entered the hospital on August 23, 1894, where he passed through a typhoid fever of very moderate intensity and without complications beyond albuminuria, with granular casts, and some epithelium. He had had measles, scarlet fever, and mumps as a child; no venereal history; used alcohol in moderation. The note on the heart states that: "The point of maximum impulse is in the fourth space, a little inside the mammillary line. Relative dulness not increased to the right. Pulse slow, of good volume and tension. Sounds clear, of normal relative intensity." No further note was made on the heart.

On January 18, 1903, the patient returned for examination. He had been well since discharge. He was rather flushed and excited; pulse, 24 to the quarter, of good size, duration fair; vessel wall just palpable. Brachial pulse visible at the bend of the elbow, and temporals visible, but not especially thickened. Blood pressure, 180 mm.

Heart. Impulse marked in the third and fourth interspaces; of maximum intensity in the fifth interspace in the mammillary line 10.5 cm. from the midsternal line. Dulness extends 3.2 cm. to the

right of the midsternal line.

At the apex the first sound is prolonged and followed by a soft systolic murmur, which is heard throughout the axilla; second clear. In the tricuspid area the sounds are clear and sharp. In the pulmonic area the first sound is prolonged and continued into a slight systolic murmur; the second, loud and sharp. The murmur is also heard in the aortic area, over the manubrium and in the carotids.

Occasionally a very slight reduplication of the pulmonic second sound is to be heard at the end of inspiration. In the erect posture a soft systolic souffle is well heard in the left back, though audible at the apex.

There may be some question as to the existence of mitral insufficiency in this case, but the high tension, the rather large size of the heart, and the audibility of the murmur in the left back are suggestive.

CASE III. Hypertrophy and dilatation of the heart; mitral insufficiency.—J. H. (Hospital No. 10,714), aged sixty-one years, was admitted to the hospital on August 24, 1894, where he passed through a typhoid fever of seventeen days' duration, of moderate severity. The urine during the attack showed a trace of albumin, hyaline and granular casts. He had had previously no serious illnesses; had used alcohol in moderation. The pulse was full, soft, regular in force and rhythm, 92. Tension not increased. Vessel wall not thickened.

Heart. Apex-beat in the fifth space, 3 cm. inside the nipple line. The first sound at the apex was occasionally followed by a soft systolic puff, not transmitted (cardio-respiratory?). Sounds at the base clear, of normal relative intensity.

On January 18, 1903, the patient returned to the hospital in answer to my letter. Up to a week before he had been fairly well. For a week he had been complaining of shortness of breath on exertion. He was somewhat cyanotic, the respirations labored and rather wheezing. The pulse was 22 to the quarter, of good size; duration fairly good; vessel wall not palpable. Blood pressure, 215 mm.

Heart. Point of maximum impulse neither visible nor palpable. By percussion and auscultation it was localized in the fifth interspace, 12 cm. from the midsternal line. Dulness 5 cm. to the right. Sounds: first, reduplicated at the apex; second, clear. The reduplication was not clearly heard in the tricuspid area. At the base the sounds were clear in both the pulmonic and aortic areas, the aortic second sharply ringing, greatly accentuated. Fine râles were heard at both bases.

The patient was admitted to the hospital on the following day, at which time the apex was found 1 cm. farther out, and a systolic murmur was audible at the apex, transmitted but a short distance outward. The sounds were feeble over the precordium. The second sounds were clear. After rest in bed the patient improved greatly. The fine râles cleared up, and eleven days later the patient was discharged. The apical murmur, however, persisted. The blood pressure in bed was 165 mm. The urine at first showed a trace of albumin, which disappeared later; specific gravity normal.

This was a well-marked case of dilatation, with mitral insufficiency.

CASE IV. Hypertrophy of the heart; mitral insufficiency.—A. B. (Hospital No. 31,173), a young woman aged twenty-four years, was admitted to the hospital on July 9, 1900, where she passed through an attack of typhoid fever of forty-six days' duration without serious complications. The urine was at all times free from albumin. As a child she had had measles, mumps, and scarlet fever, the latter followed by nephritis; the radial arteries were not palpable.

Heart. Point of maximum impulse not palpable. Sounds best heard in the fourth space, 9 cm. from the median line. First sound rather feeble. The aortic second louder than the second pulmonic.

There was no further note on the heart.

On December 22, 1902, the patient returned for examination. She had been married and had had one child since discharge. Since the birth of the child she had not felt well.

Pulse, slightly irregular in rhythm, 27 to the quarter, occasionally intermittent, of moderate size, and good duration. The vessel wall

was not palpable. Blood pressure 170 mm.

Heart. Apex impulse in the fourth space, 10 cm. from the median line. Dulness extended 3 cm. to the right of the median line. The impulse was strong, rather snapping, associated with and apparently preceded by a very slight thrill. "The first sound at the apex is rather sharp, followed by a slight systolic murmur. This murmur is heard in the axilla and faintly in the back; it is a little louder in the tricuspid area. In the pulmonic area there is a loud systolic murmur. The second sound is sharp and clear, relatively accentuated, as compared with the second aortic; no reduplication. In the aortic area there is a well-marked systolic murmur transmitted upward over the manubrium and into the carotids. The second sound is clear."

In this instance the enlargement of the ventricle and the slight irregularity of the pulse, as well as the transmission of the systolic murmur, all tend to suggest that a true mitral insufficiency exists. The snapping character of the first sound and the slight suggestion of a palpable thrill, although no corresponding murmur was to be heard, are in favor of the existence of an actual valvular lesion.

Case V. Mitral stenosis and insufficiency (?).—A. S. (Hospital No. 32,037), a girl aged ten years, was admitted to the hospital on September 3, 1900, where she passed through a typhoid fever of thirty-four days' duration, complicated by cystitis. The case was of moderate severity, the pulse not particularly rapid at any time. As

a child she had had measles, tonsillitis, and bronchitis at three years, and again the winter before entry.

In the hospital record it was noted:

"Heart. Point of maximum impulse in the fourth space, 6 cm. from the midsternal line. Both sounds well heard at the apex. Loud systolic murmur at the base. At the apex the first is accompanied by a very faint systolic murmur; the second pulmonic, not accentnated."

Later on it was again noted that there was a faint systolic murmur all over the precordium, loudest in the pulmonic area. No note was made on the heart at the time of discharge. The patient was not, however, supposed to have a cardiac lesion.

On December 22, 1902, the patient returned for examination. She had been perfectly well since discharge. The pulse was regular, 25 to the quarter, of moderate size, and rather long duration. The

vessel wall was not palpable. Blood pressure 135 mm.

Apex visible and palpable in the fourth space, 7 cm. from the midsternal line, just inside the mammillary line. Dulness 2.25 cm. to the right of the median line. The impulse was strong, rather prolonged, preceded by a suggestion of a thrill. The first sound at the apex was prolonged and booming. There was a distinct echo in the latter part of diastole, which was almost loud enough to be called a true presystolic murmur, having all the characteristics of a presystolic murmur of slight degree. The first sound was succeeded by a very soft, slight systolic murmur, which was heard in the axilla, but not in the back. Second sound well heard at the apex. In the tricuspid area there was a soft systolic murmur which became louder as one reached the pulmonic area. The second sound in the pulmonic area was sharp and clear. The same murmur was heard at the aortic orifice feebly, but better than in the pulmonic area; also over the manubrium and in the carotids. At the time "It would seem that the apex of the examination it was noted: murmur (presystolic) was doubtless produced at the time of entrance of blood into the ventricle from the left auricle, and, in all probability, at the mitral valve. The case may be one of mitral stenosis, though it is not impossible that the heart may be quite normal."

CASE VI. Hypertrophy and dilatation of the heart; mitral insufficiency; hyper-tension.—M. Z. (Hospital No. 17,636), a woman aged forty-three years, was admitted to the hospital on October 19, 1896, where she passed through a typhoid fever of sixty-four days' duration, without complications. The urine showed a trace of albumin, and once a hyaline cast. She had been previously a perfectly healthy woman, excepting for an attack of typhoid fever seven years before and for occasional pains in her joints, unassociated with fever or swelling. She had had twelve children and two miscarriages.

When in the hospital it was noted that at the apex the first sound was replaced by a soft systolic whiff, faintly transmitted to the axilla.

The second sounds were clear. The heart's action was rather irregular. The murmur could be heard all over the base of the heart. The highest recorded pulse in the hospital was 120. No further note was made upon the circulatory apparatus. On discharge the patient was considered to have a normal heart.

The patient returned to the hospital on February 16, 1903, in answer to my letter. For two months she had suffered from shortness of breath, especially on excitement and exertion. This was also worse at night, so that at times she had to sit up in bed. On physical examination the pulse was 26 to the quarter, of fairly good size; duration long; vessel wall not palpable. The blood pressure was 200 mm. The urine was free from albumin.

"Heart. Point of maximum impulse palpable in the fifth interspace, 9.50 cm. from the median line. Dulness extends 2.75 cm. to the right of the median line. Sounds: The first at the apex is followed by a well-marked blowing systolic murmur heard faintly throughout the axilla; second clear. In the tricuspid area the murmur is less marked; the second sound clear. In the pulmonic area the first sound is represented by a slight systolic murmur; the second sharp and loud. In the aortic area the first is followed by a very soft systolic murmur heard over the manubrium, not in the carotids. The second pulmonic is sharper than the second No reduplication of the second sound. In the erect posture the murmur persists at the apex, but is not heard in the back." Two months later the patient returned to the Out-patient Department again, complaining of shortness of breath. At this time the apex had moved outward 2 cm., while in other respects the signs were about the samc.

CASE VII. Hypertrophy; mitral insufficiency.—B. W. (Hospital No. 24,675), a woman aged twenty-six years, was admitted to the hospital on September 11, 1898, where she passed through a long typhoid fever, with two relapses, complicated with arthritis of the ankles. The urine was free from albumin. The patient had always been healthy and had had previously no serious illnesses. In the hospital the following note was made on the heart:

"Heart. Point of maximum impulse, fifth space, 3 cm. inside the mammillary line. At the point of maximum impulse there is a soft, blowing systolie murmur, not traceable into the axilla. Sounds at base clear; of normal relative intensity. Pulse regular; good volume; 36 to the quarter." In several notes there is no mention of palpable radials. Later it was stated that the second pulmonic was accentuated, and that the murmur was traced to the anterior axillary line.

The patient was examined on March 6, 1903, five and a half years later. After leaving the hospital there was another relapse, with left-sided femoral phlebitis. For some time afterward there was ædema of the feet. Otherwise she has been quite well. The pulse was 80, regular, of fairly good size; long duration. Artery just

palpable. Blood pressure 210 mm.

"Heart. Apex impulse in the fifth space, 10.5 cm. from the median line. Dulness extends 3.5 cm. to the right of the midsternum. At the apex the first sound is followed by a systolic murmur, which is heard all over the cardiac area, though best at the point of maximum impulse; it is transmitted as far as the mid-axilla. In the erect posture it is still heard at the apex, though with much diminished intensity. In the back as the patient sits up, it is a question whether at times a faint suggestion of a murmur may not be heard. The second sounds are both strong; the second pulmonic is distinctly accentuated."

CASE VIII. Mitral insufficiency; hypertrophy of the heart;—E. R. (Hospital No. 28,249), a colored woman aged thirty-eight years, was admitted to the hospital on Oetober 24, 1899, where she passed through a mild attack of typhoid fever of seventeen days' duration. The urine contained a trace of albumin, and hyaline and granular easts. As a child she had had measles, mumps, and chickenpox. No other serious illnesses.

In the hospital it was noted that "the point of maximum impulse is in the fifth space, 8.5 cm. from the median line. Impulse punctate, rather heaving; slight suggestion of a thrill running up to the impulse. At the point of maximum impulse the first sound is replaced by a short blow, which is preceded by a very short, indistinct rumbling. This latter is to be heard above and outside the point of maximum impulse. The systolic murmur is heard over the base. The second pulmonic is slightly accentuated and clear. The aortic second sound is clear." No note as to the palpability of the radial arteries. About two weeks before discharge it was noted that there was a systolic murmur at the apex and pulmonic areas, but on discharge it was stated that the heart sounds were clear.

On August 12, 1903, the patient returned in answer to my letter. She had had one child since leaving the hospital. For three months she has felt rather poorly, the catamenia having been profuse and of late rather irregular—possibly menopause. The pulse was regular, excepting for occasional intercurrent beats, 17 to the quarter; of moderate size, long duration. The vessel wall was just palpable on the right side; not on the left. Temporals not sclerotic. Blood

pressure 165.

Heart. Point of maximum impulse visible and palpable in the fifth space, 11.5 cm. from the median line, 1 to 2 cm. outside the mammillary line. The dulness extended 3.7 cm. to the right. Impulse, heaving, stronger than usual. "The first sound at the apex is prolonged and followed by a distinct systolic murmur heard throughout the left axilla and faintly in the back. The second sounds are sharp. In the tricuspid area the murmur is not distinctly audible. The second pulmonic is fairly sharp, and is reduplicated with about two beats

on inspiration. The second aortic is not as loud as the second pulmonic. The reduplication of the second sound is not heard in the aortic area, and is clearly due to pulmonic delay. In both pulmonic and aortic areas there is a slight suggestion of a systolic murmur, which is not heard in the carotids."

Hypertrophy and dilatation of the heart; mitral insufficiency.—J. F. (Hospital No. 36,210), aged eighteen years, was admitted to the hospital on September 9, 1901. He passed through a typhoid fever of very moderate intensity, the probable length of fever being only about thirteen or fourteen days. The uring showed a slight trace of albumin on entrance and a few coarsely granular casts, but both albumin and casts disappeared later. There were no complications. He had had chickenpox when young, but knew of no other serious illnesses. Is a farmer, and exposed to a good deal of bad weather. Does not drink nor use tobacco.

In the hospital the pulse was 21 to the quarter; marked sclerosis of radials. "Heart sounds loud and booming. Systolic murmur in pulmonic area. Second sound clear." No further note was made on the heart. The highest recorded pulse was 112. During con-

valescence the pulse was as low as 48.

In September, 1903, he reported in answer to my letter, and, in my absence, was examined by Dr. Briggs. He had been perfectly well since leaving the hospital. "Radials much sclerosed. Brachials thickened and visibly pulsating at the elbow. Pulse 24 to the quarter, slightly irregular in force and rhythm, with rare intermissions of rather short duration; large volume; not collapsing. Blood pressure 182."

Heart. Point of maximum impulse in the fourth interspace, 8 cm. from the midsternal line, though the impulse was to be felt as far out as 14 cm. from the median line in the fifth interspace, with which dulness was practically coexistent. Relative dulness extended 5 cm. to the right of the midsternal line. The systolic impulse was forcible; the shock of both sounds well felt; no thrill. At the apex both sounds were well heard, the first booming, and followed by a rather intense, blowing, systolic murmur, transmitted to the axilla, but not to the back. "In a small area upward and inward from the apex in the fourth space the second sound has at the beginning of examination a faintly rumbling echo, not running through diastole; this disappears on resting, reappearing after examination. In the tricuspid area and over the precordial region the systolic is well heard; the second sound is clear. In the pulmonic area the systolic is louder than over the right ventricle; not so loud as at the apex. The second pulmonic is louder than the second aortic and is reduplicated, the accent being on the second part of the reduplication, and the length of the interval being more marked during deep inspiration, though present throughout the respiratory phases. The aortic sound is elcar, ringing, bell-like, and, though not so loud, is more intense

than the second pulmonic. The first sound is fainter. No systolic murmur audible. There is no diastolic murmur to be heard at the

base nor along the border of the sternum."

Case X. Four months after discharge, aortic insufficiency which had disappeared five months later.—J. C. (Hospital No. 39,371), a man aged twenty-two years, entered the hospital on June 26, 1902. Here he passed through a typhoid fever of moderate severity, without complications, leaving the hospital on August 9, 1902. The urine showed a trace of albumin at the height of the disease. He had had measles as a child; denied venereal disease; habits good. In the hospital it was noted that the radial artery was palpable. On two oceasions during the disease the blood pressure was 128.

Heart. Dr. McCrae noted that the point of maximum impulse was very feeble, visible (?) in the fifth space, 10.5 cm. from the midsternal line. The first sound was everywhere of rather an indefinite

quality, but there was no actual murmur.

On November 30th, about sixteen weeks after discharge from the hospital, he reported in answer to my letter. The pulse was 27 to the quarter (the patient was rather nervous), collapsing, but of clearly high systolic pressure. Vessel wall not palpable. Blood

pressure 174 mm.

Heart. Apex in the fourth interspace, 10.5 cm. from the midsternal line. Sounds clear and strong at the apex. A soft systolic murmur was heard at the trieuspid area and at the aortic area transmitted upward over the manubrium. The second aortic sound was very loud; no murmur. Both sounds were heard in the carotids, the first prolonged as a roughened murmur. No murmur was heard in the pulmonie area. The systolic murmur was distinctly loudest at the aortic area, and was transmitted upward. There was a very soft diastolic murmur, heard along the left sternal border. This murmur was extremely slight, but was heard by Dr. Briggs, as well as by myself.

Five months later, on April 21st, the patient reported at the dispensary. He had been complaining of a slight cough, the last stage of a cold which he had had for about a week. He was still hoarse, with a teasing cough. Had not been working regularly on account of nervousness. The lungs were clear. The pulse was regular, of

good size; nothing remarkable about its quality.

"Heart. Apex impulse not seen nor felt. By stethoscope and percussion it was localized 9.5 cm. from the median line, in the fifth space. Dulness extends 3.5 cm. to the right of the median line. At the apex and all over the eardiac area, most marked in the aortic area, there is a soft systolic murmur, which wholly disappears in the erect posture. The sounds are otherwise clear, excepting that in the pulmonic area there is a reduplication of the second sound, which occurs several times during ordinary inspiration, the delayed part being clearly the second pulmonic. This reduplication is heard at

times in the aortic area. There is no diastolic murmur either in the erect or recumbent posture."

The case is one of much interest. May it have been an instance of transient dilatation of the aortic ring?

Case XI. Aortic insufficiency.—L. R. (Hospital No. 20,507), a man aged thirty-nine years, was admitted to the hospital on September 4, 1897, and passed through a typhoid fever of fifty days' duration, followed by a relapse, associated with bronchitis and a pemphigoid eruption on the hands. The urine contained no albumin, but an occasional hyaline and granular cast was found. As a child he had had scarlet fever, and almost every fall had had malarial fever. Four years before entry he had had another attack of typhoid fever; four years before, urethritis. The pulse was not remarkably rapid at any time during the course, and the only note with regard to the circulatory apparatus was "heart negative."

On February 15, 1903, the patient reported in answer to my letter, and, in my absence, was examined by Dr. Briggs. The patient had been well since discharge, but had lived a life of hard work and exposure. "Pulse 82; slightly irregular in force and rhythm; distinctly collapsing; vessel wall moderately thickened; marked visible pulsation in brachials and carotids; none in the temporals. Marked capillary pulsation. Systolic blood pressure, 185 mm.

"Heart. Point of maximum impulse just visible and palpable in the fourth space, 12 cm. from the median line, in the left mammillary Impulse faint; no thrill. The relative dulness begins at the second left interspace and extends to the right sternal margin at the level of the fourth rib. No absolute cardiac dulness. At the apex both sounds are heard; the first rather muffled, followed by a soft systolic puff, carried to the mid-axilla, and faintly heard at the xiphoid. The second sound is sharp and clear. Just above the nipple, in a small area, there is a short, faint rumble in diastole. ending before the first sound, which is not snapping. Both sounds are heard over the right ventricle, with a systolic murmur, which becomes more marked in the second, third, and fourth left spaces, and is heard at the base, though not over the manubrium, and in the neck. The pulmonic second is louder, accentuated; occasionally a faint reduplication with inspiration. The aortic second is soft, but clear. În the second and third left interspaces close to the sternum there is a very short, faint diastolic murmur following the second sound."

Case XII. Marked arterio-sclerosis. C. Z. (Hospital No. 17,632), a boy aged thirteen years, was admitted to the hospital on October 19, 1896, where he passed through a typhoid fever of seventeen days' duration, without complications, being discharged on November 19, 1896. There was a trace of albumin, with hyaline and gran-

ular casts, during the height of the fever. He had suffered from no previous serious infections, and, so far as could be determined, was a boy of good habits. The highest recorded pulse in the hospital was 112. A full note on the heart was made by Dr. McCrae. Pulse 21 to the quarter, soft, and easily compressible; synchronous in radials and femorals.

Heart. Point of maximum impulse in fourth space, 7 cm. from the median line; wavy; no thrill. Area of cardiac dulness not increased. Sounds: A soft, systolic murmur was heard at the apex, not especially carried around to the axilla; best heard over the second and third left spaces. The second sound was very loud at the apex and much accentuated in the second left space. No further note as to the heart.

On January 4, 1903, he returned in response to my letter. Three years ago he had had an attack of tonsillitis, after which his tonsils were removed. Beyond this he had considered himself quite well. The pulse was 25 to the quarter, showing rather marked irregularities in rhythm; of good size and long duration. The vessel wall was much thickened; readily rolled under the finger. The temporals were tortuous, prominent and somewhat thickened. The systolic pressure was 200 mm.

Heart. The apex impulse was visible and palpable in the fifth space just inside the mammillary line, 8.7 cm. from the median line. The dulness extended 3.2 cm. to the right of the midsternal line. Sounds. The first at the apex was prolonged and booming, followed by a very slight systolic murmur, which was lost before one reached the mid-axilla. "A much more distinct, high-pitched, blowing systolic follows the first sound in the tricuspid area and over the right ventricle in the third and fourth spaces. It is, however, barely audible in the pulmonic area, and is not heard in the aortic area or over the manubrium. It is not affected by change of position. Sounds at the base clear. The second aortic is accentuated." At the time that this note was made the following remarks were added: "In this instance there is a distinctly hypertrophied heart, with marked sclerosis of the radials and temporals. The murmur heard in the tricuspid area is not of the ordinary character of a functional murmur, being higher pitched and having a very blowing sound."

This case, it seems to me, is one of particular interest, in view of the fact that beyond the tonsillitis the only element to which one could reasonably ascribe the cardio-vascular abnormalities was the preceding typhoid fever.

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#### SUMMARY.

A study of the condition of the heart and vessels in 183 individuals who have passed through typhoid fever at the Johns Hopkins

Hospital within the last thirteen years has revealed the following facts:

- 1. The average systolic blood pressure in these old typhoids was appreciably higher than in control observations upon healthy individuals.
- 2. The higher average of the blood pressure was constant in every decade.
- 3. In many instances among the old typhoids the blood pressure exceeded appreciably the limits of what is usually regarded as normal.
- 4. The radial arteries in the old typhoids were palpable in a proportion nearly three times as great as that found in control observations upon supposedly healthy individuals who had never had the disease.
- 5. The average size of the heart was greater among the old typhoids than in the same cases at the time of admission to the hospital. The difference held good also when the cases were classed according to age by decades.

6. Cardiac murmurs were heard with considerably greater frequency among the old typhoids and in the same cases during the

attacks.

- 7. In 8 cases where, on discharge from the hospital, the heart was considered normal, subsequent examination revealed hypertrophy, with mitral insufficiency. One case showed a possible mitral stenosis; one an aortic insufficiency; one a striking general arteriosclerosis, with hyper-tension.
- 8. In one case an aortic diastolic murmur was present four months after discharge, but had disappeared five months later.
- 9. Those patients whose pulse during the disease was remarkably rapid or irregular, showed, in general, on later examination, a blood pressure above the common average for the old typhoids. In other respects, however, their condition differed but little from the general run of cases.
- 10. Those cases in which a systolic murmur at the apex of the heart was observed during the attack showed later an increase in the blood pressure and in the size of the heart, as compared both with the mean of the observations made upon the same cases on admission to the hospital and with the general average for the old typhoids. Nearly one quarter of those cases in which during the attack, systolic apical murmurs were detected, showed, on later examination, evidences of organic heart disease. Indeed, the majority of all the cases of organic cardiac lesions among the 183 old typhoids came from this small group of 31 cases.

It is recognized that these results are based upon the analysis of a number of cases too small to justify final conclusions; the next 200 cases may considerably modify the figures. Yet the fact that these 183 old typhoids are materially older, from a point of view of their hearts and arteries, than the average individual who has not had typhoid fever, would tend to support the views of those who regard this disease as an active element in the ætiology of a considerable number of cases of cardiac hypertrophy and dilatation coming on sometimes in early life, as well as an important factor in the production of those vascular changes which Cazalis has happily called "la rouille de la vie."

#### MULTIPLE SARCOMA.1

### By Thomas A. Claytor, M.D.,

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This subject is one so broad that it becomes of interest alike to

the internist, the surgeon, and the dermatologist.

The particular class of cases which I propose to consider is that in which there are multiple sarcomatous growths in the skin and subcutaneous tissue, excluding that class of tumors characterized by lymphoid cells, in which are included leukæmia, pseudoleukæmia, and malignant lymphoma, and also the so-called sarcoid group, comprising idiopathic hemorrhagic sarcoma, sarcoma cutis, and multiple benign sarcoid. Cases have been reported in which the tumors seemed to have been multiple from the beginning, but it seems more probable that there was a primary growth which may have escaped notice, so rapidly was it followed by an outburst of metastatic tumors. The secondary growths may be pigmented or non-pigmented, or may be mixed—i. e., some may show melanotic material, while others are entirely white, which was observed in one of my cases to be reported later. They may belong to the round, spindle, or myeloid form of sarcoma, or the cells may change from one form to another during the progress of the disease. The tumors usually appear as small, round nodules, the size of a shot, which rapidly develop into oval or round plates, which may be somewhat depressed in the centre. The size to which they may grow is indefinite; as a rule, however, few reach a greater diameter than one inch. They are situated either in the skin proper, or in the deep fascia, hence may move with the skin or the skin may move freely over them. Ulceration may occur either from pressure or from apparently spontaneous breaking down of the new tissue. They may or may not be encapsulated. The latter condition is said to improve the outlook. The appearance of the cutaneous or subcutaneous nodules is either preceded or rapidly followed by involvement more or less

<sup>1</sup> Read before the Medical Society of Washington, D. C., October 7, 1903.

general of internal organs and tissues, which in a longer or shorter time, usually the latter, causes death.

After a careful study of a number of reported cases, I find it unprofitable to attempt any statistical classification of the seats of primary growth, there being apparently no special points of predilection

The primary growth may be a pigmented mole situated anywhere upon the skin; it may be in the subcutaneous tissue, or may spring apparently from the bone, skull, vertebræ, etc., or from an internal organ.

The following reports of cases, two of which I have observed myself and the others selected from the literature, will give a clearer

idea of this most fatal affection:

CASE I.—R. C., white, male, married, aged thirty years, butcher, was admitted to Garfield Hospital December 4, 1902. His father died of pneumonia; his mother is living and in good health. C. had the usual diseases of childhood, including measles, mumps, whooping-cough, etc., from which he made good recoveries; had enteric fever when fifteen. He went to school until he was twelve, and then worked for ten years in a factory. Since then he has been a butcher. Three years ago he had erysipelas extending over the scalp, face, and neck. The attack resulted from a scalp wound. Immediately after this a swelling was noticed on the right side of the head in the occipital region, which increased in size very slowly until the present time, when it is about the size of a large walnut. For the past eighteen months the stomach has been irritable, the meals being frequently vomited. These periods have been intermittent, however, and at times his stomach gives him no trouble. The vomitus has never contained blood. Had gonorrhœa eight years ago, but has never had syphilis. Uses no alcohol. He was married six years ago, but his wife has borne no children.

The present attack may be dated from the first appearance of the tumor on the back of his head, which was three years ago. The growth of the tumor has been intermittent, there being periods when it did not seem to enlarge for some time. No other enlargement was noted until last May, seven months ago, when a nodule began to develop on the right side of the neck about two inches below the mastoid process. This gradually increased in size until two months ago, when it seemed to diminish a little. In July another nodule appeared under the skin near the umbilicus. The tumor on the neck caused pain and stiffness until it stopped growing. About this time, because of his general debility and anæmic appearance, he was advised to take a trip to California. About September 1st nodules began to appear on the chest and a few on the abdomen. None of them gave any pain and moved freely under the skin. Nodules then appeared on the right arm and in the right axilla. Those in the axilla gave pain, with a feeling of contraction. Later the growths appeared on the left arm. About October 15th slight swelling of the abdomen was for the first time noted, which has gradually increased. Complains of pain across the shoulders and chest, which keeps him from sleeping. There is no cough, but considerable

dyspnœa on slight exertion.

Physical Examination. Emaciated and anæmic. In the right posterior occipital region is a tumor about the size of a walnut, which is just beneath the scalp, very slightly movable on the skull, and of almost bony hardness. This is probably the primary growth which was first noticed three years ago. Numerous smaller nodules may be felt in or under the scalp. On the right side of the neck, rather toward the posterior aspect, is a firm, nodular tumor, three and fivetenths inches long by three inches in the anteroposterior diameter. About the periphery are numerous smaller nodules. The large tumor is quite firmly fixed, though it is not absolutely so, the smaller ones being freely movable. There are nodules in the left postcervical region; there is a small nodule situated over the inner third of each clavicle. Numerous small nodules are seen upon the anterior aspect of the right arm, one upon the right forearm. The right cpitrochlear gland is slightly enlarged. There are numerous small nodules extending from the right axilla down to the ilium; also in the right interscapular, right lumbar, and sacral areas posteriorly and on the right side of the chest anteriorly. One tumor, larger than the rest, about half an inch in diameter, two inches to the right of the umbilicus. One situated about midway between the umbilicus and ensiform cartilage, about a quarter of an inch in diameter, is red, and is said to discharge pus from time to time. This is the only tumor which seems to be attached to the skin, all the others apparently growing from the deep fascia, being alike freely movable upon the muscles and under the skin. Growths are also seen in and about the left axilla, upon the left arm, left side of the chest and back, but are not so numerous as upon the right side. A few nodules are upon the right thigh and in the right inguinal region.

The growths vary in size from a shot to a large marble, except the primary growth on the head and the first secondary on the neck; some are plate-like, others round. They are firm, elastic, and not painful. There is no discoloration of the skin, except over the one situated on the abdomen, near the umbilicus, which has broken

down.

The pulse is weak and compressible. No abnormality is to be discovered in the heart or lungs; the liver and splcen cannot be satisfactorily examined because of a large ascitic collection. (These

organs were found at the autopsy not to be enlarged.)

Between the date of the first examination and that of the patient's death numerous hard masses, about the size of a fist, were detected in the abdominal cavity. They seemed to be quite freely movable in the ascitic fluid and were proven at the autopsy to be sarcomatous masses in the omentum.

The patient said that the nodules first appeared about the size of a pinhead and gradually increased without pain, except when they were subjected to pressure against a bony surface.

One of the smaller growths was removed on December 11th. It was eneapsulated. The following is the report by Dr. J. B. Niehols:

Alveolar, large, round-celled sarcoma. Areas of beginning necrosis seattered irregularly throughout. Blood examination showed 3,710,000 reds, 6300 whites, hæmoglobin 65 per cent.; no abnormality in size or shape of red eells. A differential eount of the white cells showed: small mononuclears, 13.8 per cent.; large mononuclears and transitional, 8 per cent.; polynuclear neutrophiles, 78 per cent.; eosinophiles, 0.4 per cent.; mast-cells, 0.8 per cent.

The urine showed no abnormality, except a rather high specific

gravity.

Examination of the stomach contents after an Ewald test breakfast showed: total acidity, 31; acidity due to HCl, 11; free HCl,

0.04 per eent.; lactic acid, 0; pepsin deficient, etc.

The most distressing symptoms were due to the rapid and persistent accumulation of ascitic fluid. For twenty-four to forty-eight hours after a tapping there would be comparative comfort, only to be followed by intrathoracie pain, nausea, vomiting, dyspnœa, etc., as the fluid accumulated. The temperature was irregular, ranging from subnormal to 100° F.; the pulse and respirations were never frequent.

Death occurred on January 29, 1903, about three years after the appearance of the primary growth beneath the sealp, and about nine months after the appearance of the first secondary growth, which was on the right side of the neck, and about four months after general

subeutaneous involvement.

Necropsy. Multiple, hard, subeutaneous nodules (for size and situation see ease history). Emaciation extreme. Heart: weight, 265 grams; small; fat diminished, musele dark red. Myoeardium of every ehamber contains deeply pigmented nodules situated subendoand subperieardially and intramurally, varying in size from a pea to a hazelnut. Valves normal, eoronaries patulous, aorta slightly atheromatous. Perieardium contains a few eubic eentimetres of straweolored fluid. Lymph glands frequently sareomatous. Spleen: weight, 171 grams. One nodule at the hilum, two of larger size deep in the splenie substance. Right lung: weight, 285 grams. Moderately pigmented; a small, easeous, firmly eneapsulated area in the apex; interlobular adhesions; two subpleural sareomata over middle lobe; a few small sarcomata in the lower lobe, one large tumor at the root. Left lung: weight, 250 grams. A few nodules in the lower lobe, otherwise negative. Stomach: mueosa congested. Small intestine: sarcomatous nodules generally distributed over serous coat. Large intestine: a large nodule situated at the ileoeæeal valve. Subperitoneal sarcomata everywhere; a nodular mass at the splenie flexuræ.

Peritoneum: moderate amount of straw-colored fluid. The omentum solid, firm, dark red; a mass of sarcomatous nodules 4.7 cm. at the thickest portion. Liver: weight, 1550 grams; two small nodules on the peritoneal aspect of right lobe; in the substance of the lobe are four nodules. Kidneys: the only point worthy of note is the difference in size and weight of these organs; the right weighs 170 grams, the left 57 grams.

Unfortunately, there could be no examination of the brain or cord. Treatment consisted of hypodermic injections of Fowler's solution twice daily, beginning with three drops. The X-ray was also tried, but neither had any beneficial effect, though there was an increase in the number of red cells and in the hæmoglobin until a short time before his death. The subcutaneous nodules continued to appear, and the internal growths increased in size. That the primary growth was that of the right occipital region I see no reason to doubt, and whether or not its prompt and complete removal would have changed the outcome is the important question.

Case II.—A. S., male, white, aged twenty-eight years, brakeman, was admitted to the University Hospital July 7, 1903 (on the service of Dr. W. P. Carr, by whose courtesy I have been allowed to observe and report the course of the disease). One grandfather died of tuberculosis, otherwise the family history is good. He was a healthy child; had measles at three and typhoid fever at twelve, from which he made good recoveries. Uses tobacco freely and drinks a great deal of coffee, but no alcohol. He has had no venereal disease. Went to school until he was sixteen and since has worked. Has always been strong and healthy until the beginning of the present illness. Last February he began to feel languid and at about the same time noticed for the first time a nodule behind the left ear on the mastoid process. The growth increased in size and was removed in the middle of

Two other nodules had already appeared on the chest when the growth over the mastoid was removed, and these were rapidly followed by others. On June 2d one of the nodules was excised for diagnostic purposes. It was found to be a large round-celled sarcoma, the picture being very similar to that in the previous case. On July 8th Dr. Carr removed the recurrent growth, which had extended well down on the lateral aspect of the neck, had broken down, and was giving considerable trouble. At the same time he removed a number of the subcutaneous growths from the chest and upper abdomen.

July 21st the red cells numbered 4,312,000, whites 18,000; the hamoglobin was 60 per cent. A differential count showed: large mononuclears, 11 per cent.; small mononuclears, 5 per cent.; polynuclears, 72 per cent.; eosinophiles, 11.5 per cent.; myelocytes, 0.5 per cent. I am unable to account for the eosinophilia. The urine was negative.

Symptoms. The chief trouble from the beginning in February was weakness. There was abnormal pain and occasional nausea and

vomiting.

Physical examination July 28th showed marked paleness and emaciation. Over the chest, back, and abdomen were numerous nodules, varying in size from a shot to a small marble. There was no discoloration of the skin over these nodes, which were not painful to the touch, except those which had been subjected to the X-ray. They were freely movable, being for the most part subcutaneous, moving on the muscle and under the skin. Some, however, were attached to the skin. There were a few growths on the arms, thighs, and legs. The heart was in its normal position, but there was a systolic murmur, heard with greatest intensity at the apex and transmitted into the axilla. The lungs were apparently normal, though there was an area of dulness at the base of the right lung, which may have been due to an upward enlargement of the liver. The latter organ extended two inches below the costal border. A large, hard mass, the size of the double fist, was felt in the median line of the abdomen, just above the pubes. Between this and the umbilicus another smaller mass was felt. Neither was painful. The spleen could not be felt. As to which was the primary growth, it may be said that the one over the mastoid was first noticed, but the abdominal pain began at about the same time, and the abdominal mass was of large size. The small nodules continued to multiply, and the patient left the hospital in September, and has since died. His illness lasted about seven months from the appearance of the primary growth.

The X-ray was also used in this case without curative effect.

J. Sabrazès and L. Muratet¹ report a case, in a man aged sixty-six years, of very general involvement, which was fatal in eight months. The previous history showed nothing worthy of note. Following a supposed attack of grip, there appeared a small growth below the right clavicle, which was rapidly followed by a multiplicity of tumors over the body. At the same time tumors developed in the abdominal cavity. The growths under the skin varied in size from a shot to large nodules, raising the skin, and readily made out by palpation. The principal parts involved were the trunk, upper portion of the arms, and face, while the forearms, legs, and feet were free. Death occurred after eight months, during which time the tumors continued to increase. The autopsy showed the growths to have developed in the subcutaneous connective tissue. The skin was movable over them. There were also tumors on the long bones of the upper extremities or adherent to the periosteum, in the kidneys, and in the pericardium and myocardium. The blood count showed only 8060 leukocytes.

Levi<sup>2</sup> reports a case of melanotic sarcoma in a man aged fifty

<sup>1</sup> Arch. dc méd. expér. et d'anat. path., 1902, vol. xiv.

<sup>2</sup> Bull, soc. anat. de Paris, 1899, lxxiv.

years. The primary growth was situated on the inner surface of the fourth toe on the left foot. It was first noticed when about the size of a pea. As the man was a baker and went without his shoes a great part of the time, it was thought that some traumatism was probably the cause. The disease, which had begun six months previously, extended rapidly to the neighboring toes, thence to the groin, where a hard tumor, the size of a fist, formed. The primary growth broke down and ulcerated. Small black nodules like the primary one appeared on the leg and in the popliteal space. During the later stages small melanotic subcutaneous nodules appeared on the outer surface of the right thigh, the edge of the right upper eyelid, the scalp, etc. Signs of pulmonary involvement then were noted, and a vague delirium, with prostration, preceded death.

Autopsy showed melanotic nodules involving the subcutaneous cellular tissue. Numerous sarcomatous nodules, both melanotic and

non-melanotic, were found in the lungs, kidneys, and brain.

J. H. Musser¹ reports an interesting and frequently quoted case of universal melanotic sarcoma in an old woman, who, on January 19, 1878, had had the right eye removed for supposed glaucoma (probably sarcoma). She was readmitted in September, 1887, with a small tumor on the left side of the neck, which was painless, slightly elastic, about the size of a walnut, adherent to the skin, the surface of which was bright red and puckered. One week later another tumor was found on the right arm, it was subeutaneous, not so red or as prominent as the former. Other tumors rapidly developed, most of them on the trunk and upper extremities, a few on the thighs. They were more abundant on the right half of the body. A great number were movable under the skin, some adherent to it, and presented a reddish hue. They were abundant in the scalp. She died March 4, 1888, about six or seven months after the appearance of the tumor on the neck.

The autopsy showed involvement of nearly all the internal organs, including the heart, lungs, liver, adrenals, ovaries, uterus, etc. There was no examination of the brain or cord.

D. Grant<sup>2</sup> gives a partial report of the following interesting case: A man, aged twenty-seven years, gave a history of having had a black mole on the deltoid of his right arm since birth. Three years previously it had been wounded by the horn of a sheep, but soon healed; some time afterward it was hurt again, and then spread to the size of a finger-tip. Eighteen months after receiving the first injury it was bruised again, and this time did not heal readily. A few additional small patches appeared in close proximity. The whole area was then excised. This was the end of June, 1896. In November a lump appeared in the right axilla, which was excised, but since a large number of growths in the skin have appeared over

<sup>&</sup>lt;sup>1</sup> Philadelphia Hospital Reports, 1893.

<sup>&</sup>lt;sup>2</sup> Intercolonial Medical Journal, Melbourne, Australia, 1897, ii.

the trunk, both front and back. The general health was excellent, but the condition was considered so grave that he was sent to the Pasteur Institute to receive the Coley treatment. This is a striking example of the serious results which may follow injuries to congenital moles

Charles F. Withington¹ reports, among others, a case of multiple sarcoma, in which the primary growth had existed twenty or thirty years without giving any signs of malignancy. It occurred in a man aged seventy years, of good personal and family history. Six months before admission he noticed a number of small black tumors on the surface of the body, which had increased since then. About the same time he began to lose weight and strength. It was then learned that he had had for twenty or thirty years a tumor on the posterior aspect of his shoulder, non-pigmented and painless. Death occurred only six or seven months after the secondary tumors appeared. Autopsy showed extensive metastasis in the brain and internal organs, especially the heart.

F. C. Shattuck<sup>2</sup> reports a wonderfully rapid case, in which death occurred in less than four weeks after the appearance of the subcutaneous nodules. There was extensive involvement of the internal organs. The primary growth was thought to have been in the dorsal

vertebræ.

ETIOLOGY. Concerning the cause of sarcoma, whether single or multiple, practically nothing is known. It may follow an injury or may take its origin from old scar-tissue, or there may be no discoverable cause. The parent tumor in the variety of multiple sarcoma now under consideration is not infrequently a pigmented mole, which suddenly takes on the characteristics of a malignant growth. The usual cause for this change is an injury accidentally sustained or friction from the clothing. It may be as well to state here that it has been shown by several authorities, notably Chambard, J. Hutchinson (Jr.), Unna, and Gilchrist (Crocker), that all melanotic growths are not sarcomata, and Unna states that all growths with metastasis which start from pigmented moles are really melanotic carcinomata rather than sarcomata. The clinical behavior, however, is the same.

Concerning the pathology, I shall say nothing.

SYMPTOMATOLOGY. The symptoms are not distinctive. Besides wasting, there are likely to be those which arise from the presence of

tumors, such as pain, ascites, etc.

The blood, so far as I know, shows nothing except the conditions found in any severe secondary anamia. My case (II.) had a leukocytosis of 18,000, but at the time the examination was made there was a suppurating wound.

DIAGNOSIS. In a fully developed case, with more or less widely scattered subcutaneous nodules, the diagnosis is simple, especially after once having had one's attention called to the condition. In the

<sup>&</sup>lt;sup>1</sup> Medical and Surgical Reports, Boston City Hospital, 1897.

<sup>2</sup> Boston Medical and Surgical Journal, 1894.

early stages, however, when, as is often the case, there appears an irregularly nodular bunch on the side of the neck, with, perhaps, a few small nodules in the neighboring lymphatic areas, there are several possibilities which suggest themselves, namely, leukæmia, pseudoleukæmia, lymphosarcoma, tuberculosis, or syphilis. The fact that all of these conditions involve the lymphatic glands, and hence are found in lymphatic areas only, is of diagnostic importance, for the sarcomatous growths are not confined to these localities. In fact, they are usually in greatest abundance on the outer surfaces of the arms, on the chest, etc., localities where lymphatic glands are not found. Lymphatic leukæmia may be excluded by a blood examination, the other possibilities only after observation of the case for a longer or shorter time, depending on the rapidity of the appearance of metastatic growths. The most satisfactory method is to remove one of the smaller nodules for microscopic examination. This very simple procedure is, however, not without danger, since operations upon sarcomata are often followed by rapid and more malignant recurrence. If the skin has been involved the growth is almost sure to recur at the original site, but if subcutaneous the danger is much less.

TREATMENT. The rational course would seem to be that of prompt and complete removal of all suspicious growths, especially if they show the slightest signs of activity. It is a fact, however, that in many of these cases the extirpation of the primary growth is so quickly followed by an outburst of secondary tumors that we are forced to ask ourselves if the operation did not act as a stimulant to a more or less quiescent condition, and in that way only hasten the inevitable result. The question of operation, then, is one which

requires careful consideration.

So far as drugs are concerned, arsenic is the only remedy which has proven of any value. Köbner's¹ case is frequently referred to as an example. He gave Fowler's solution hypodermically, at first from 2¹₁ to 4 drops daily, diluted with an equal volume of water, to an eight-year-old girl, who suffered from multiple sarcoma. The treatment was begun September 12, 1881, and was continued with increasing doses (up to 9 drops) until January 5, 1882. The nodules decreased greatly in number and size and the enlargement of the liver and spleen decreased. The treatment was continued until March, 1882, and in January, 1883, the condition was much improved; the body weight had increased; there were only a few nodules in the skin, and these were much less pigmented.

Sherwell's<sup>2</sup> case showed improvement, but the patient was unable

to continue the use of the arsenic, and died.

Other cases of great improvement or of apparent cure have been reported from time to time from the use of arsenic, but the outlook under any circumstances is very dark.

<sup>&</sup>lt;sup>1</sup> Berliner klin. Wochensch., 1883.

<sup>2</sup> THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, vol. civ.

# TUBERCULOUS STRICTURE OF THE ASCENDING COLON, WITH SUDDEN TOTAL OBSTRUCTION OF THE BOWEL; PERFORATION OF THE INTESTINE; REMOVAL OF THE CÆCUM AND HALF THE ASCENDING COLON; RECOVERY.

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The careful and exhaustive articles bearing on lesions of this character that have already appeared render it superfluous for me to enter into a detailed consideration of the subject. Before describing the present case, therefore, I shall merely enumerate briefly the salient pathological and clinical features of the disease. Those wishing to study the subject fully are referred to the interesting articles of Henri Hartmann and Pilliet, and Reclus, in the French; of Hofmeister, Adolf Hartmann, and Gross, in the German, and of Lartigau, in this country. Hofmeister has tabulated all the cases he could find in the literature, and his consideration of the subject is most thorough, while Baumgarten, through his students, Hartmann and Gross, has contributed not a little to the pathological aspect of this disease. The works of Lartigau and Hofmeister should be carefully read by all particularly interested in this class of cases.

Tuberculous ulceration of the intestine is relatively frequent, as evidenced by the findings at autopsy, but stricture of the lumen of the bowel following as a result of this condition is somewhat rare. Hofmeister says that Eisenhardt, in 1000 autopsies on tuberculous patients, found intestinal lesions 566 times. In only 9, however, was there a more or less definite stricture of the bowel.

Tuberculous strictures of the bowel are usually single and situated at the ileocæcal valve. The cæcum is converted into a sausage-shaped mass, which is adherent, as a rule, posteriorly and occasionally laterally. The omentum, although at times adherent to the growth, is not as prone to engraft itself on the tumor as in cases in which appendicitis exists. The outer surface, while relatively smooth, may be studded by a few tubercles. At one point the gut shows a constriction, and usually around this the adipose tissue is very dense. Where the cæcum is cut into the mucosa frequently shows considerable alteration. It is sometimes studded with irreg-

<sup>&</sup>lt;sup>1</sup> Note sur une variété de typhlite tuberculeuse simulant les cancers de la région, Bull. de la Soc. anat. de Paris, 1891, vol. lxvi. p, 471.

<sup>&</sup>lt;sup>2</sup> Typhlite et appendicite tubcrculeuses, Cliniques Chirurgicales de la Pitié, 1894, p. 317.

<sup>&</sup>lt;sup>3</sup> Ueber multiple Darmstenosen tuberkulösen Ursprungs, Belträge zur klinischen Chirurgie, 1896, Bd. xvil. S. 577.

<sup>4</sup> Ein Fall von tuberkulöser Darmstenose, Inaug. Diss., Tübingen, 1897.

<sup>&</sup>lt;sup>5</sup> Ueber Stricturirende Darmtuberkulose, Inaug. Dlss., Tübingen, 1901.

<sup>6</sup> Journal of Experimental Medicine, 1901, vol. vi. p. 23.

ular or serpiginous tuberculous ulcers, while the intervening mucous membrane is the seat of a chronic inflammatory process. At the point of stricture the lumen of the gut is so narrow that the tip of the finger can hardly be introduced. In some cases so small is the calibre of the bowel that a sound is passed with difficulty, and in our case a small bird-shot was sufficient to completely occlude the canal. The degree of alteration in the cæcum varies with the individual case, and it is only necessary for the reader to picture the tuberculous process advancing until the cæcum becomes matted and densely adherent to all the neighboring structures, and, in rare instances, the process gradually involves the abdominal wall until finally there is a fistulous opening on the surface. Even in the early stages the mesenteric glands are enlarged and already involved in the tuberculous process, and where the cæcal invasion is apparently in its incipiency there may be caseation of these glands.

Tuberculous stenoses of the gut, when multiple, are almost in-

Tuberculous stenoses of the gut, when multiple, are almost invariably situated in the ileum. Anywhere from one to twelve strictures have been noted in the same patient. In one case Hofmeister found twelve strictures scattered over a distance of about seven feet of gut. The bowel between the strictures is frequently distended, and in rare cases has been known to reach 17 cm. in circumference. Lartigau draws especial attention to a group of these cases, in which, associated with the tuberculous process, there is a marked diffuse thickening of the bowel wall, which occasionally

reaches 1 cm. or more in thickness.

The appendix is usually adherent, but, except where the tuberculosis of the cœcum is far advanced, shows no implication in the specific process. Our case proved no exception to the rule. Although bound down by adhesions, the appendix was otherwise normal.

HISTOLOGICAL PICTURE. In sections from the cæcum the edges of the ulcers may show tuberculous tissue, but, as a rule, epithelioid cells or typical tubercles are wanting, and nothing but granulation tissue can be made out. In the vicinity of the muscle, however, groups of epithelioid cells, and now and then tubercles, are seen. The peritoneal surface is usually free from tuberculous nodules until the disease is far advanced or unless the cæcal lesion has been associated with tuberculous peritonitis. Sections from the stricture are composed entirely of connective tissue; sometimes with, at other times without areas even slightly suggestive of tuberculosis. The adipose tissue surrounding the gut at the point of stricture is much infiltrated with small round cells, rendering the fat exceedingly hard and firm. Sections from the lymph glands in the region of the cæcum almost invariably yield typical tubercles.

cæcum almost invariably yield typical tubercles.

Naturally the tuberculosis gradually extends to the muscle and outer coats of the bowel. The farther away the process extends from the lumen of the bowel, the more characteristic will be the specific lesions, since the inflammatory changes produced by the

intestinal bacteria have less opportunity of masking the tubercles. The diffuse thickening or "chronic hyperplastic tuberculosis" of the intestine yields a very different picture to that of simple tuberculosis, as has been clearly pointed out by Henri Hartmann, Lartigau, and others. In these cases the tuberculous process has been relegated entirely to the background, while the mucosa and muscle have been overrun with round cells. Intestinal bacteria have doubtless gained entrance to the walls through the tuberculous lesions and have continually kept up a chronic inflammation of the bowel wall so widespread in character that the tuberculosis is entirely overshadowed. Ât a few points, however, it will still be demonstrable, and can be detected with certainty in the mesenteric lymph glands. Even in the cæcal wall, when the typical lesions are totally wanting, tubercle bacilli can still be readily demonstrated.

CLINICAL HISTORY. Patients presenting tuberculosis of the cæcum are usually between twenty and thirty years of age. The condition, however, may be found in the very young, and has been noted in persons fairly advanced in years. Quite commonly the patient has suffered from an old tuberculous process in the lungs or has a suspicious family history. In many of the cases which have come to autopsy healed lesions in the lungs have been demonstrated, while in a few instances there has been swelling of the cervical, axillary, or other lymph glands coincident with the cæcal lesion. One of the first symptoms is constipation. After a time dull or sharp pain is felt in the appendiceal region. As the constriction develops there may be an intermittent diarrhea, with the gradual narrowing of the bowel, and fulness may be noted over the cæcum. Where there is much infiltration of the intestinal wall the gut becomes very firm and feels like a sausage-shaped tumor. With the gradual growth of tuberculous tissue and narrowing of the bowel symptoms of obstruction manifest themselves, as evidenced by abdominal distention, colicky pain, marked peristalsis, vomiting, and rapid loss in weight.

But although these symptoms may be present, in some instances definite indications of the presence of the lesions may be entirely absent. In our case the patient felt well until the day before operation, complaining only of slight discomfort near the appendix.

DIAGNOSIS. With the increased attention paid to caecal tuber-culosis the possibilities of overlooking these lesions will be lessened. It was only a few days after our case was operated upon that Dr. Finney saw a patient giving symptoms sufficiently suggestive of a tuberculous lesion in the cæcum to render such a diagnosis justifiable. At operation the cæcum was found to be the seat of a most extensive tuberculous ulceration. Fortunately, it was found possible to excise the whole of the diseased area.

Given a tumor in the right iliac fossa of slow growth, a clinical history pointing to a previous pulmonary tuberculosis, and a comparative absence of temperature, it is highly probable that tuberculosis is present. If a patient be fairly well advanced in years, of course, the possibility of a malignant growth must be considered. As pointed out by Hartmann, Lartigau, and other authorities, tuberculosis of the execum, especially of the hyperplastic form, has often been taken for sarcoma. This has been due to the massive infiltration with small round cells. But provided that we remember that they form a definite infiltration, instead of one or more large foci, and further, that the cells are uniform in size instead of being large and small and actively dividing, confusion is not likely to occur.

The gross diagnosis between tuberculosis and carcinoma of the cæcum may offer numerous difficulties, but on microscopic examination no confusion can exist, as in the tuberculous process the epithelial elements play an entirely passive rôle or have disappeared. Moreover, the demonstration of the tubercle bacilli is generally easy.

The diagnosis between cæcal tuberculosis and appendicitis is usually dependent on the tuberculous history and the slow growth of the tumor, together with the absence of a temperature suggestive of a pus accumulation. Of course, in a case similar to the present

one, a differential diagnosis would be absolutely impossible.

TREATMENT. If tuberculosis of the cæcum be diagnosed early operation is indicated. Resection of the entire diseased area is, of course, necessary for an absolute cure. Lateral anastomosis between the ileum and ascending colon is the ideal operation. If after resecting the diseased portion of the gut very little mobility be obtainable, in order to avoid tension an end-to-end anastomosis is the only alternative. Where there are numerous strictures scattered over an area of several feet of gut, the question arises as to whether the entire diseased area be excised or several anastomoses be made, removing only the diseased segments and leaving the intervening normal gut. If the span of gut involved by the tuberculous process be not over three or four feet, it is wiser to remove this portion in its entirety. In one of the cases reported between six and seven feet were removed, and the patient recovered. With the diseased cæcum it is always necessary to carefully examine the glands of the mesentery, and if they be involved, they too should be excised. The results from resection have been very gratifying, Hofmeister in his table of 83 operative cases showing a recovery of 62 per cent.

Tuberculous stricture of the ascending colon, with sudden total

obstruction of the bowel; perforation of the intestine; removal of the cæeum and half the ascending colon. Recovery.—The following is taken from my case-book, November 29, 1902: At 11 p.m. I saw, in consultation with Dr. Charles E. Simon, Miss K. G., aged twenty-four years. The day before she had indefinite pains in the region of the appendix. They were, however, not very severe and lasted but a short time. To-day she did her work as usual and prepared supper, but shortly afterward was taken with severe pain in the right side and was forced to go to bed. At 9 P.M. Dr. Simon saw her.

There was marked rigidity of the right rectus over the appendiceal region. There was little temperature. On examination of the blood Dr. Simon noted that all eosinophiles had disappeared and that there was an evident leukocytosis. When I saw her two hours later the rigidity of the right side had in part disappeared, probably as she was slightly under the influence of morphine. The general condition was good; pulse full and regular. Nevertheless, I advised immediate operation.

At 1.30 A.M. the abdomen was opened and a thin, watery pus immediately escaped from the peritoneal cavity, and the pelvis was found to be completely filled with pus. The intestinal loops, however, on the whole, presented a fairly normal appearance. Here and there they were covered by a few flakes of fibrin. The appendix was easily recognized and was bound down by adhesions. It was tied off from tip to base. As the distal extremity appeared to be normal, we expected to find a perforation near the cæcum, but on complete removal of the appendix it was found that, apart from adhesions, no alteration was present. After removing the pus from the abdomen a sponge was passed into the right renal pocket to see if any pus was there, and, to our surprise, some dark fluid escaped. This was entirely different from that found in the pelvis. The abdominal incision was continued upward to the ribs, and we immediately saw a perforation, about 4 mm. in diameter, in the ascending colon. As there was a good deal of fluid escaping, I temporarily closed this fistulous opening with a purse-string suture. I then drew the ascending colon out and made a longitudinal incision, and on introducing the finger into the colon found total obstruction a short distance above the ileocæcal valve. The lower third of the ascending colon, the cæcum, and a small portion of the ileum were tied off and removed, together with some enlarged glands in the mesocolon. The ascending colon and ileum were then united by end-toend anastomosis. Lateral union would have been preferable, but we had no choice, as the tissues would have been on too great a tension. A Connell suture was employed for two-thirds the circumference of the gut, the remaining third being turned in with rectangular mattress sutures. The entire line of suture was reinforced by running mattress sutures. The pelvis was carefully sponged out, the intestinal loops brought up into the abdomen, and the entire pelvis loosely packed with iodoform gauze.2

<sup>&</sup>lt;sup>1</sup> Simon lays much stress on the frequent absence of cosinophiles where pus is accumulating, and thinks that this sign is of more practical value than the degree of leukocytosis.

<sup>&</sup>lt;sup>2</sup> For several years, where the pelvis has been filled with free pus, I have made it a practice, after having wiped the pelvis and intestines off, to place the patient for a moment in the Trendelenburg posture. The pelvis has then been loosely but fully packed with gauze, the ends of which are brought out through the appendix incision. My object has been to prevent the intestinal loops from dropping down and becoming adherent or kinked in the pelvis. In my hands this procedure has yielded very gratifying results. The loops, although still liable to become adherent, are on a level and are not nearly so prone to become obstructed.

A gauze drain was also left at the site of the anastomosis. The patient stood the operation well. Her pulse did not rise above 100. The outlook, however, was not particularly flattering, considering the fact that there was a commencing peritonitis and also considerable cedema of the intestinal wall. Eight days after operation, on removing the last of the gauze, some fecal matter was found on the dressing. The fistula gradually closed, and the patient made an excellent recovery.

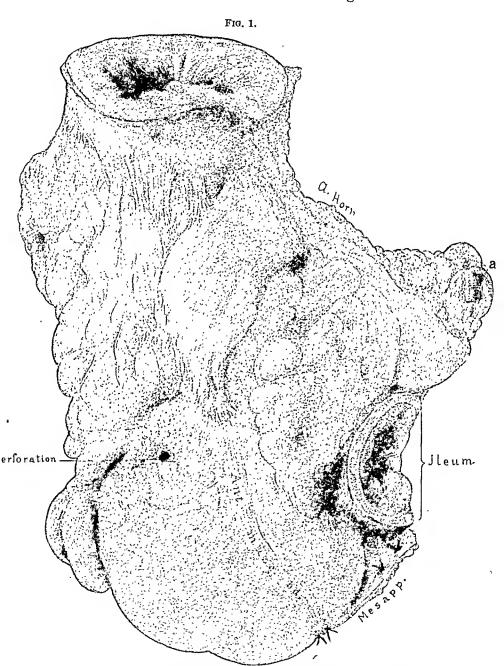
February 12, 1904. The patient has been at work for several months, performing general household duties without the slightest inconvenience. Her general condition is excellent. From her I learned that she had had typhoid (?) fever six years previously and was in bed for two weeks. For the last year she has had cramp-like pains throughout the abdomen two or three times a month, and recently the bowels have been more constipated than usual. She gives no history whatever of injury or bruising of the abdomen. For about a week before her admission to the hospital she had had intermittent abdominal pain. From the family history we were unable to get any data suggestive of hereditary tuberculosis.

Pathological Report. (Gynecological Pathological No. 6316.) The specimen consists of a small portion of the ileum, of the cæcum, and of about one-half of the ascending colon. The mucosa of the ileum is unaltered, that of the cæcum in most places is normal, but at a point directly opposite the ileocæcal valve is a perforation 5 mm. in diameter (Fig. 1). The walls of the perforation are rather smooth and the surrounding mucosa, over an area 1 cm. in diameter, is somewhat thickened. The ascending colon, about 5 cm. above the perforation, shows a marked constriction. At this point the lumen narrows down until it is not more than 2 mm. in diameter. Indeed, so small is it that a finc bird-shot would lodge and completely plug the canal at this point (Fig. 2). The intestinal wall at the point of constriction varies from 5 mm. to 8 mm. in thickness and is exceedingly firm in consistence. The constriction is 1 cm. in length and the ascending colon above this point is unaltered.

Histological Examination. The appendix, beyond showing a few adhesions on its outer surface, is normal. The execum in the vicinity of the perforation has entirely lost its glandular elements, the specimen consisting almost entirely of granulation tissue. The underlying muscle shows a varying amount of small round-celled infiltration. This is especially abundant in the vicinity of the peritoneal covering.

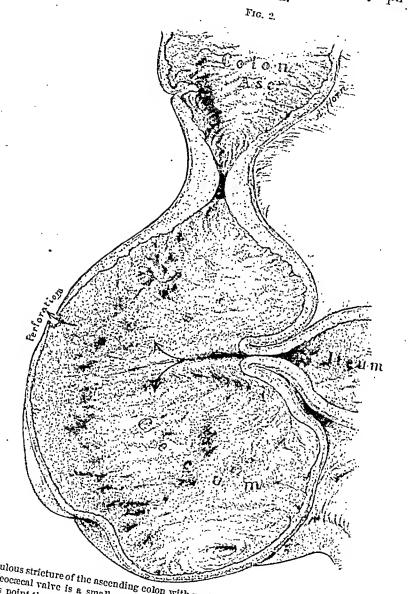
Along the margin of the perforation there is also much granulation tissue, and the underlying muscle is everywhere infiltrated by small round cells. The ulceration is evidently an old process, as nowhere is a very acute inflammatory reaction present. The walls of the stricture are, to a great extent, composed of fibrous tissue. Here and there we have some light areas somewhat sug-

gestive of tuberculosis. No giant cells are, however, demonstrable. Several mesenteric glands were removed with the intestine. Some of these reached 1.5 cm. in diameter. On histological examination



Tuberculosis of the excum with perforation (natural size). Above is a cross-section of the ascending colon. Below and to the right the ileum. At a point directly opposite the ileum is a perforation of the excum, and just above the perforation the adipose tissue is thickened and there is a constriction of the gut. At a are two enlarged and tuberculous lymph glands. For the interior view of the specimen, see Fig. 2.

these show typical tubercles, some sections of which contain four or five giant cells. The tuberculous process in the lymph glands has here and there advanced to cascation. FIG. 2.



Tuberculous stricture of the ascending colon with perforation of the execum. Directly oppo-Tuberculous stricture of the ascending colon with perforation of the execum. Directly opposite the fleocecal valve is a small perforation with slightly ragged edges. A short distance above this point the intestinal walls grow thicker and then form an annular constriction.

The lumin of the according color at the efficience has been so performed that a small like. The lumen of the ascending colon at the stricture has been so narrowed that a small birdshot, when introduced, lodged therein and completely plugged the gut.

The following points merit attention in this case:

1. The total absence of definite symptoms until a few hours before operation.

- 2. The presence of symptoms identical with those of acute appendicitis.
  - 3. Marked contraction of the stricture.

4. The advisability of always exploring the right renal pocket in all cases in which there is free purulent fluid in the pelvis.

As seen from the history, the patient had practically no symptoms until about five hours before operation, and then there was moderate pain over the appendix, accompanied by rigidity of the

right rectus.

Examination of the blood showed a total absence of eosinophiles. The only way in which we can account for the lack of symptoms is that for some reason there occurred an acute contraction of the stricture, which, up to this time, had permitted the free passage of feces. The possible existence of such a condition supplies another indication for early operation whenever trouble exists in the appendiceal region. Already peritonitis had developed, although the symptoms had existed for so short a time; and had we delayed until morning there would have been little chance of saving the patient.

After having removed the appendix and wiped the pus from the pelvis, the abdominal cavity appeared normal, and I probably should not have explored the right renal pocket had I not been familiar with the renal work of Max Broedel, who has shown clearly that where there is a free accumulation of fluid in the region of the appendix that by gravity it will travel down into the right

renal fossa.

I should have preferred lateral anastomosis, but we were forced to make an end-to-end union on account of tension.

## A STUDY OF NORMAL AND PATHOLOGICAL CONDITIONS OF THE BURSÆ OF THE NECK, WITH SPECIAL REFERENCE TO THE SUBHYOID BURSA.\*

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We find on searching the literature of the older writers references to cystic tumors of the neck, some of them, no doubt, of bursal origin; but from the descriptions given it is impossible to know their exact nature. Commencing with Celsus, who mentions tumors of the neck,

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down to the latter half of the eighteenth century, we find occasional references to these conditions; but not until the beginning of the nineteenth century can we find any definite literature on the subject.

Boyer, in his treatise published in 1831, describes cysts of the neek as follows: "There is sometimes found between the hyoid bone and the thyroid eartilage, upon the membrane uniting them and behind the thyroid musele, an encysted tumor, containing a viscous, yellowish fluid." He further states that they usually eause no trouble except that the deformity may be annoying, especially to women. While Boyer's cysts are undoubtedly hygroma of the subhyoid bursa, he did not recognize them as such, nor did he seem to have any knowledge of the existence of a bursa normal to this region. Voillemier and Vidal appear to have had a vague knowledge of its existence, but Malgaigne,2 in 1838, was the first to describe accurately this bursa. Verneuil,3 in 1853, published a eareful study of the bursæ of the neck and their affections under the title "Recherehes anatomiques pour servis a l'histoire des Kystes de la partie supérieure et médiene du cou." In this monograph he gives the location of the different bursæ found in this region. The most complete study of the subject the writer has found is a thesis by Batut, published in 1886.

Besides the above-mentioned, a few scattered articles in German, French, and English have been found, and an occasional brief reference in some of the more complete works of surgery.

The fairly constant scrous bursæ of the neck, according to Verneuil, are three in number: 1. Subcutaneous antethyroid, also called præthyroid. 2. Deep subhyoid (Boyer's bursa). 3. The superficial or sushyoid.

The subcutaneous antethyroid bursa, described by Beclard, lies in the loose areolar tissue over the Adam's apple. This bursa is not always present, and when existent it varies in size from a mere space to a well-defined sae easily demonstrated. It is difficult to differentiate any bursa in the loose tissue in women and children; in men it is usually present and tends in both sexes to grow larger as age advances. It develops as the result of friction between the subcutaneous tissue and the prominence of the thyroid eartilage.

The subhyoid bursa, described by Malgaigne, is the one more directly to be considered. It is situated between the hyoid bone and the thyrohyoid membrane. Superiorly, it is limited by the insertion of the thyrohyoid membrane to the lower lip of the upper border of the body of the hyoid bone; anteriorly, its wall is formed by the posterior surface of the hyoid bone at its upper portion and the cervical aponeurosis below; posteriorly, it is limited by the thyrohyoid membrane; inferiorly, it reaches to the upper portion of the thyroid cartilage by an infundibuliform prolongation; laterally, it may extend under the thyrohyoid muscle, but its usual limit is the inner border of

the muscle. It is about 2 cm. long by 1 cm. broad, and larger in men than in women and children. Verneuil found it rudimentary in a fetus, and constantly present in fifteen adult subjects. The subhyoid bursa is rarely absent. Malgaigne describes it as a single sac, with two lateral prolongations, while the more accurate dissections of Verneuil show it to be a double bursa, with a partition in the median line. The latter observer explains the development of this double bursa as the result of friction between the upper border of the thyroid cartilage and the hyoid bone, and, because of the thyroid notch in the median line, less friction is experienced at this point, a fact which accounts for the median wall of connective tissue separating the two bursæ. There is sometimes a connection between the antethyroid bursa and the subhyoid bursa.

The superficial or sushyoid bursa described by Verneuil lies between the geniohyoid and the geniohyoglossal muscles. Besides the three above-mentioned bursæ, which are fairly constant, others have been found and described by various observers. Among these may be mentioned a second bursa lying in the concavity of the hyoid bone, described by H. Luschka. Fleichman described a bursa on the geniohyoglossi next to the frænum of the tongue as the bursa sublingualis. Rosenmüller, quoted by Luschka, described the bursa sternohyoidea between the sternohyoid muscle and the hyoid bone. Others have been described as the thyroidea lateralis (Gruber), stylohyoidea, cricothyrothyroidea (Calori), and thyrotrachealis (Calori).

While considering the location and structure of this bursa, mention ought to be made of the remains of the thyreoglossal duct. There is in the embryo (His)8 a prolongation of the thyroid gland upward, forming a duct or tract. This tract runs (Butlin) from the foramen cæcum at the base of the tongue downward in the raphé between the geniohyoglossi muscles to the hyoid bonc. It is infimately connected with the body of the hyoid bone, with its periosteum, and with the subhyoid bursa behind. Below the mylohyoid muscle the tract can be traced from its close connection with the lower and posterior edge of the hyoid bone downward in front of the thyrohyoid ligament to the pyramidal lobe of the thyroid gland beneath the raphé uniting the sternohyoid muscles. This tract may remain open in a portion of its extent, which accounts for the cysts of this duct. There is found frequently in its course small masses of thyroid gland tissue, . which are known as the accessory or parathyroids. This duct is lined by ciliated epithelium, and is in close relation with several bursæ of the ncck, especially the subhyoid bursa.

The gross anatomy of the burse of the neck has been studied by a number of observers, but there does not seem to have been any attention given to their histological structure. The writer has made a number of dissections of subhyoid burse, with the object, first, to confirm the work of other observers; and, second, to demonstrate the histological structure of these sacs. Several dissections of embryos and children at term show the bursa in a very rudimentary state. On gross inspection all that is evident are the small spaces in the very loose areolar tissue lying between the body of the hyoid bone and the thyrohyoid membrane. Dissections from one subject, examined histologically with a low power, revealed a fair-sized space in the loose areolar tissue. There was no distinct limiting membrane lining the whole of the cavity, but in places with a high power there was a suggestion of such a limiting membrane lined by flattened endothelial cells. It would seem that in early life this bursa was nothing more than a mere space in the areolar tissue without a distinct lining membrane. The bursa in adult subjects was regularly found larger in men than in women. It occupied considerable space in the loose tissue behind the hyoid bone. The interior of the sac was smooth, and had the appearance of a serous lining: In some cases trabeculæ could be seen running across the cavity. Histologically, no continuous lining could be demonstrated, but in places a limiting membrane lined by flattened cells was observed. The lining membrane was much more distinct in the specimens taken from the children at term. In no instance were columnar ciliated cells found.

The results obtained from this limited study are in harmony with what we should expect from our knowledge of subcutaneous bursæ in general. Since these bursæ develop as the result of friction between the adjacent parts, we should expect them to vary considerably in size and structure, and also to be more developed in advanced age. Schafer10 says: "It must, however, be observed that among the subcutaneous bursæ some are reckoned which do not always present the characters of true synovial sacs, but look more like mere recesses in the subcutaneous arcolar tissue, larger and more defined than in the neighboring areolæ, but still not bounded by an evident synovial membranc. These may be looked upon as examples of less developed structure, forming a transition between the areolar tissue spaces and the perfect synovial cavities; indeed, it may happen that what is a well-developed synovial bursa in one subject is merely an enlarged areola in another. Many of the bursæ do not appear until after birth, and they are said to increase in number as age advances. The synovial membranes are composed entirely of connective tissue with the usual cells and fibres of that tissue. There exist on the synovial membranes no complete lining, although patches of cells may, it is true, here and there be met with which present an epithelioid appearance."

No definite etiology of cysts of the subhyoid bursa has been found. It is thought that trivial traumatisms, so slight as to escape the memory, may be the cause. Tight collars, especially when the edges press at that point, may be the exciting factor. The latter cause is the one given by a patient who consulted the writer. They are never congenital.

Symptoms. As a rule, these cysts cause but few subjective symptoms. The symptoms are proportionate to the size of the tumor, and are caused naturally by the mechanical presence of the growth. If the cyst is small no inconvenience is felt; the larger ones sometimes interfere with deglutition or respiration and give rise occasionally to a sense of stiffness of the muscles of deglutition. In rare instances cysts have attained such a size as to give rise to serious symptoms. One author claims that these swellings may be visible on the floor of the mouth, but it would seem that this was an error in diagnosis, as the thyrohyoid membrane, which limits the upper border of the bursa, is a firm resisting membrane. The cysts develop slowly and are not painful or tender to the touch. They vary in size from a slight swelling to a tumor the size of an orange. Usually they are the size of a hazelnut. They are found just below the hyoid bone, in the median or just to one side of the median line, and they are firmly attached to the underlying tissue. The tumor is usually globular and tense; the skin over it freely movable, and shows no sign of inflammation. They are usually smooth, but in long-standing cases a roughened surface has been detected. Fluctuation may be present, depending on the size of the growth, the contents, and the possibility of fixing the tumor while the sign is being elicited. They are said to be more common in men. The cases seen by the author were in females, but the sensitiveness of women to any deformity may account for it apparently being more common in them. In the few cases reported where the cysts have attained a larger size, there are, in addition, pressure symptoms, which may give rise to interference with circulation in the neck, to dyspnœa, or to dysphagia.

The clinical history of these cases varies. They may remain for years, causing but little inconvenience and not increasing appreciably in size; they may disappear under treatment so simple that one feels that the treatment was not the cause of their disappearance. Such was the fact in one of the writer's cases, although it has been claimed by some that they never disappear spontaneously. They may vary in size from month to month, as in one case now under observation. They may spontaneously open, or open as the result of local treatment, and leave a chronically discharging sinus. They may become

The differential diagnosis between the hygroma of the subhyoid bursa and other tumors of the neck ought not to be difficult in the majority of cases. It can be distinguished from a cold abscess by the absence of induration at the base and by the freedom from evidences of inflammation and constitutional symptoms. Its situation above the thyroid cartilage will easily differentiate it from ordinary enlargement of the thyroid gland. An enlarged lymphatic gland would be unusual in the median line, although a single lymphatic gland has been demonstrated in this region. As a rule, enlarged glands are situated at the side of the neck, and are dependent upon tuberculosis.

infected and form an abscess.

syphilis, or some point of infection in the nose and throat. Aneurysms of the neck give rise to pulsating tumors, which easily distinguishes them from cysts, although the possibility of the pulsation from a vessel transmitted through a tumor must be remembered. the tumor can be moved toward the median line and drawn away from the vessel the pulsation will cease. If the possibility of lipoma must be eliminated, this can be done by an exploratory puncture. Sebaceous cysts are indolent, inflammatory swellings, with a black point at the summit of the swelling, and the integument is closely adherent. Cystic swellings of other bursæ must be differentiated by their situation. The diagnosis between median branchial cysts, thyroglossal cysts, and cysts of the subhyoid bursa is more difficult, and much confusion exists. A study of the literature and reported cases of cysts in this region shows that a clear distinction between the various cysts has not been made. The important diagnostic point is the histological structure of the sac. If the wall of the sac is lined by ciliated epithelium, the cyst is a branchial or thyroglossal duct cyst; if lined by flattened endothelium, it is of bursal origin. Such examination ought to be made in every case. Branchial cysts in this region have a pedicle adherent to the hyoid bone.

The two cases seen by the writer were probably hygroma of the subhyoid bursa. It is to be regretted that no histological examination of the wall of the sac could be made. The diagnosis was made

by the location, the character, and appearance of the swelling.

Case I.—Girl, aged twelve years. Family and personal history has no bearing on the case. Five or six months previous, before she came under observation, her mother noticed a lump on the child's throat in the region of the hyoid bone. At first it was small, but it grew gradually larger. No history of traumatism or other etiological cause was obtained. The tumor at no time gave rise to any symptoms referable to the interior of the throat, except, perhaps, a little stiffness on swallowing. The general health of the child was excellent. Examination showed a tumor about the size of a marble, which lay in the median line, on a level with or just below the body of the hyoid bone. The tumor moved with the hyoid bone, but it did not seem to be attached to the body of this bone, as it could be moved independently of the bone. The growth was circumscribed, and to the touch was of a cystic nature. The skin was not adherent, and there was no evidence of inflammation. The parents declined operative treatment. About a year later the patient was seen, and the tumor was found to have completely disappeared. The father reported that the tumor had remained stationary for several months and then, without treatment, had gradually grown smaller. possibility of this being a cyst of the thyroglossal duct or a parathyroid, which developed about the time of puberty, cannot be excluded.

Case II.—Woman, aged forty-three years. Referred to the writer by Dr. W. R. Parker. General health good. About five years before

consulting the writer she noticed a swelling just to the right of the median linc of the neck, about on a level with the hyoid bone. There was no enlargement of the thyroid gland. The patient thinks the pressure of a high collar may have caused the swelling. There was observed no relation between the growth and her menstrual function. Examination showed a cystic tumor about the size of a large marble, situated just below the hyoid bone, as if it came out from under the body of that bone. The skin was freely movable over the growth, and there was no induration at its base, nor signs of inflammation. There were no constitutional symptoms, nor any subjective symptoms, except possibly a little stiffness on swallowing. As the patient did not wish any operative interference, she was advised to use tincture of iodine locally. The tumor decreased in size and remained so for about a year, then increased again, and later again diminished. It has never entirely disappeared. She does not think the variation in size has been the result of treatment.

A careful study of the literature on this subject shows that comparatively few cases of undoubted bursal cysts have been reported, and in still fewer cases has a microscopic examination of the sac proven beyond doubt their bursal nature. Any attempt to tabulate the cases reported would be unprofitable, because so much uncertainty exists as to the exact nature of many of the cysts of the hyoid region. These cysts are probably not so rare as the meagre number of cases reported would indicate. The following, cited by various writers, compose the bulk of cases found after careful search. It is evident that some of the cases are not of bursal origin.

Three cases are quoted by Batut:4

CASE I.—Male, aged twenty-three years, had a seromucous cyst of subhyoid bursa, about the size of a pigeon's egg, situated a little to the right in the thyrohyoid region. It contained a viscid, stringy, serous fluid. It was unsuccessfully treated by an injection of tincture of iodine and alcohol, but was finally cured by a single injection of chloride of zinc.

Case II.—Male, aged twenty-four years; tumor, the size of a hazelnut, situated above the thyroid cartilage, in the median line of the neck. Various methods of treatment were used, but a chronic discharging fistula resulted.

CASE III.—Male, agcd twenty-nine years; tumor, the size of a walnut, situated to the right of the median line. The contents of sac was a mucous fluid, which contained no pus or epithelial cells. The tumor was completely extirpated, but later the patient died of cedema

of the glottis.

Dressel<sup>11</sup> describes at length a case in a girl aged eighteen years. Preceding the fistula there was a cystic tumor, the size of a hazelnut, above the thyroid cartilage. As a result of local applications the cyst opened and a chronic fistulous tract resulted. A study of the lining of the membrane of this tract proved that it was lined by

ciliated epithelium, and he rightly concluded that the case was a fistula following a cyst of the remains of the thyroglossal duct, and not a subhyoid bursa. This author quotes thirteen cases gathered from various sources, but on studying their histories it is not easy to tell definitely the nature of the cysts. In none of the cases was the cyst wall examined microscopically. Cholesterin crystals were noted in the contents of the three cases.

Dr. A. Friedlowsky<sup>12</sup> describes a case of cystic degeneration of the subhyoid bursa. It was more prominent posteriorly and pushed the epiglottis backward. It was a small, firm, round tumor, filled with a viscid, amber fluid. The walls were tolerably thick. It was found to be a degeneration of the subhyoid bursa. No microscopic examination was made of the sac.

Dr. R. F. Weir<sup>13</sup> reports a case of the extirpation of the subhyoid bursa. It returned after being tapped and injected with iodine. He emptied the cyst with a trocar, injected melted paraffin, allowed it to solidify, and then dissected out the whole cyst. He speaks of the value of this method, which enables one to dissect out the entire cyst wall, and thus prevent a persistent fistula.

In the London Lancet<sup>14</sup> a case is reported as a subhyoid dermoid cyst in a girl aged twelve years. The tumor was noticed for five or six years; it gradually increased in size, and it was situated in the median line. On opening the cyst it was found to pass backward and behind the hyoid bone. The contents consisted of oily matter and crystals of fatty acids. No microscopic examination of the sac was made, but it was described as resembling mucous membrane. The author assumed that it was lined by columnar, ciliated epithelium and that it was a dermoid. It is to be regretted that a microscopic examination of the wall of the sac could not have been made, as this may have been a case of a cyst of the subhyoid bursa.

Ingalls<sup>15</sup> reports a case, in a male aged thirty years, of a hemispherical growth, about one inch in diameter, situated just above the thyroid cartilage, and causing no inconvenience. History of syphilis several months before. The growth was movable and slightly fluctuating. An exploring-needle proved it contained pus. The diagnosis of a suppurating bursa was made, the fluid was withdrawn, and a 5 per cent. to 10 per cent. carbolic solution was injected.

Result not given.

Dr. Hamilton, 16 in a paper on "Supralaryngeal Encysted Tumors of Bursal Origin," reports ten cases. No examination of the walls reported. They contained a thin yellow serum. Dr. Elsberg, in the discussion of the above paper, reported three cases. He also referred to the dissections he made of the bursæ. He found the bursal space either with or without distinctly developed membranous walls. The cysts contained a watery serum, varying in consistency and color, more or less viscid, synovial or mucoid. They usually contained cholesterin crystals, a large quantity of albumin,

and the soluble salts of the blood. Besides the above-mentioned, cases have been reported by Malgaigne, Boyer, Roguette, Hyrtl, and others.

It is the general experience that these cysts do not spontaneously disappear of their own accord, but, on the contrary, have a tendency to become inflamed and to open by ulceration. This gives rise to a chronically discharging fistula, which may persist indefinitely, causing much annoyance to the patient.

The different methods of treatment may be divided into:

1. General and local absorbents.

2. Simple incision and drainage.

- 3. Drainage and the use of a local irritant to produce adhesive inflammation.
  - 4. Partial excision of the cyst wall.

5. Complete extirpation.

- 1. There is no reason to believe that the internal use of diuretics, iodides, mercurials, or other absorbents have any beneficial effect in bursal affections. The local use of absorbents, irritants, or vesicants seldom does any good, although an occasional report favorable to their use can be found. In a case which the writer reported above the cyst disappeared entirely without treatment. No local application should be used that will cause inflammation or vesication, as a chronic fistula has followed too active local treatment.
- 2. Simple incision with drainage is of no avail. If the incision closes, recurrence is the rule; if it remains open a chronic fistula is the result.
- 3. Drainage of the sac and the use of local irritants to produce closure has been tried successfully in a number of cases, but failures are also reported. In some cases a chronic suppurating fistula, with all its annoyances, has resulted. The method is a familiar one in surgery and depends on the ability to obliterate the entire sac by adhesive inflammation. The cause of the failure seems to be that the local irritant cannot be brought into contact with all parts of the sac or that a too strong application is followed by suppuration, which persists with the development of the fistula. When it is recalled that the sac normally extends up behind the hyoid bone, narrowing as it ascends, and is usually prolonged downward to an infundibuliform prolongation, we can understand why it is not easy to obliterate the whole sac. Incision and cauterization of the wall with nitrate of silver, chloride of zinc, or caustic potash, have been tried and good results reported. Solutions of iodine, carbolic acid, alcohol, chloride of zinc have been used as injections, with varying results. Panus cured a case by injecting a solution of chloride of zinc into the sac without evacuating it. This lessons the danger of severe inflammatory reaction.
- 4. Partial extirpation of the cyst is unsatisfactory and not to be advised.

5. Complete extirpation of the cyst is by far the most satisfactory method of treatment, although in Boyer's time he considered it impossible. Difficulty has often been experienced in dissecting out the entire sac. Weir's method is an excellent one. He injected the sac with melted paraffin, and allowed it to harden before attempting to dissect out the sac. This method allows the cyst to be shelled out entire.

The writer wishes to acknowledge his indebtedness to E. H. Hayward, who prepared the histological sections at the Detroit Clinical Laboratory.

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### HÆMOLYMPH NODES.1

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THE earliest mention of the occurrence of nodes macroseopieally resembling the spleen was that of Leydig, in 1857, who described their occurrence along the abdominal aorta. Since 1875 the presence of lymph nodes of a red color or containing red blood cells has been noted by a number of observers, and various explanations have been offered to interpret these findings. To Warthin, of the University of Miehigan, we are indebted for the most systematic and extensive study of these structures, and in his recent articles are contained the most convincing proof of the existence of the so-called hæmolymph node as an organ sui generis.

It is not the purpose of the writer to review exhaustively the work of others in this field, or to describe in detail the histology of these nodes, but rather to present the results of a personal study of their

A study from the Department of Pathology of the College of Physicians and Surgeons, Columbia University, New York.

individuality and functions. A summary of the work of others in this field had been prepared, but the literature has since been so satisfactorily abstracted by Warthin in his most recent publication that this and the complete bibliography are omitted. The histology is well presented in his other articles.

These so-called hemolymph nodes have been found by various observers in man, monkey, ox, sheep, goat, horse, pig, dog, cat, weasel, ferret, stoat, rabbit, squirrel, rat, mouse, bat, water-vole,

mole, fowl, and turkey.

The structures denominated hemolymph nodes vary in size from that of a pinhead to that of a lymph node, though averaging smaller than the latter. They are dark red, brown, or mottled red and white, usually smooth, soft, and elastic, but easily ruptured. Few or many bloodvessels surround or enter the nodes, in some cases at a hilum. Lymphatics are apparently absent in some cases. When ruptured the nodes resemble a blood clot. possesses a delicate capsule of connective tissue with some nonstriated muscle fibre. Just within the capsule is a peripheral blood sinus from which irregular prolongations run throughout the node. Between the sinuses are cords of lymphoid tissue, and usually cell collections resembling lymph follicles toward the periphery of the node. In some cases the division into cortical and medullary portions is very indistinct, and the relative amount of lymphoid tissue is generally smaller than in a lymph node. The sinuses are traversed by an irregular reticulum, usually finer than that of a lymph node, this and the sinus walls apparently being lined with endothelium. Proliferation of the endothelium appears to furnish the large phagocytes lying in the sinuses and in some cases nearly filling them. An artery enters at and a vein emerges from the The artery divides into branches which run in trabeculæ extending from the capsule through the sinuses. The finer branches sometimes appear to terminate in the sinuses; others break up into capillaries in the lymph cords, some of these capillaries apparently emptying into the sinuses. The sinuses terminate in veins which unite into one, emerging at the hilum. In some nodes small arteries enter at various points in the capsule, and in the transition forms afferent lymphatics may be seen entering the peripheral sinus. In some transition cases the blood and lymph sinuses seem to be separate systems; in others bloodvessels and lymphatics appear to mingle their contents in common sinuses. The sinuses contain varying numbers of red cells, either free or in various stages of disintegration within the phagocytic cells already mentioned, and leukocytes. The characteristic feature is said to be the occurrence normally, in the sinuses of a node, of destruction of red cells which have been brought to the node by bloodvessels.

The various interpretations which have been placed upon the presence of red blood cells within the sinuses of structures re-

sembling lymph nodes, or the occurrence of bodies macroscopically suggesting accessory spleens or red or mottled lymph nodes, are that they are: (1) neoplasms; (2) masses of newly formed splenic tissue; (3) lymph nodes engaged in the formation of new red cells; (4) lymph nodes whose sinuses contain blood as the result of congestion, hemorrhage, diapedesis, absorption of extravasated blood, etc.; (5) hemolymph nodes.

The interpretation as neoplasms was advanced by but one observer, Mosler, who described the dark-red nodules found in the greater and lesser omenta of a splenectomized dog and termed them "hemorrhagic telangiectatic lymphomata." Their microscopic structure was the same as that described by others as hemolymph nodes. Tizzoni and others have interpreted them as newly formed splenic tissue, basing their view upon their occurrence in animals the spleens of which they had removed. The investigations of Morandi and Sisto, and of Warthin appear to have conclusively disproved the splenic nature of these nodules. The idea that the lymphoid nodules with sinuses containing red cells were structures engaged in the formation of red blood corpuscles has been supported by a number of the earlier observers, but recently by Retterer only. Some were led to this belief by finding in the sinuses large cells containing what appeared to be red blood cells, some of which they described as being extruded. These are now generally regarded as endothelial cells displaying phagocytic activity and ingesting the red cells. Retterer believes that lymph nodes produce blood plasma, leukocytes, and red cells, the last derived from lymphocytes by a hæmoglobin change of the nucleus. The evidence of all other investigators appears to disprove this construction of the presence of red cells. The view that the appearance of red cells in the sinuses is due to hyperæmia, hemorrhage, diapedesis, or the absorption of extravasated blood by normal lymph nodes has been advocated by several writers, of whom Saltykow is the most decided representative at present. His study of the subject has been careful and systematic. Examination of sixty autopsy cases has convinced him that the red nodes are merely lymph nodes whose sinuses contain blood brought by lymph vessels from regions in which hemorrhage has occurred, or entering them by diapedesis from capillaries in the node, or by homorrhage from them into the lymphoid tissue or sinuses, the presence of red cells in the sinuses exciting the endothclial cells of the latter to intense phagocytic activity. His reasons for assuming that the nodes are merely lymph nodes are: in a large proportion of the cases an extravasation of blood is found in the node itself or the surrounding cellular tissue; in many nodes the vasa efferentia and subcapsular sinus are the only or chief containers of red cells, giving the impression that they are filled from without; the red nodes are found in the situations of normal nodes, and all transition forms to the ordinary type exist.

The interpretation as organs sui generis, variously denominated hæmolymph, hæmal, and hæmolytic nodes, dates from the time of Gibbes' preliminary report in 1884. Since the present writer began his investigations the ground has been covered with remarkable unanimity by Morandi and Sisto, Weidenreich, Lewis, and Warthin, to whose articles he would refer those desiring the bibliography, review of the literature, and full description of the histology. They agree that the hæmolymph nodes are a distinct set of organs whose functions are the production of leukocytes, and especially the destruction of red cells and to a less degree of leukocytes. Morandi and Sisto give as their reasons for ascribing to these organs a hæmolytic function the constant occurrence in their sinuses of cells containing red cells in various stages of disintegration, and the increase of those phagocytic cells after splenectomy, and still more after subsequent administration of hæmolytic substances. The writers mentioned agree also that there is a complete series of transition forms from the structure of the spleen to that of an ordinary lymph node. Warthin regards them as a set of structures subject to variation, one form passing into another as the needs of the body require. He describes the formation of new hæmolymph nodes as beginning with angiectatic dilatation of the capillaries of a fat lobule, the fat cells becoming enlarged, the capsule of the lobule thickened. Lymphocytes are infiltrated along the walls of the capillaries; fat cells are absorbed, and some are converted into reticular cells; proliferation of endothelium in the dilated capillaries divides them into Continued lymphoid formation, development of sinuses, and absorption of fat complete the transition into a hæmolymph node. Progressive hyperplasia of lymphoid tissue encroaching upon the sinuses may transform this or a previously existing hæmolymph into a lymph node.

In the writer's own investigations hamolymph nodes have been observed and studied in the adult, infant, dog, cat, red deer, rabbit, and guinea-pig. Failure to discover them in the gray squirrel was

probably due to incomplete examination of a single subject.

In all experimental cases the nodes were removed immediately after death and fixed in Orth's or Zenker's fluid, alcohol, or formaldehyde solution. Celloidin was usually employed for embedding, occasionally paraffin. Hæmatoxylin and eosin were ordinarily used in staining. The experimental work was confined to the dog and rabbit, the normal condition of these animals being verified by autopsy and microscopic examination.

### I. Evidence in Favor of Other Interpretations than Organs Sui Generis.

In support of the view that red cells in the sinuses are brought by afferent lymphatics from regions in which there is extravasation of blood is the fact that in a number of cases in which the sinuses of nodes contained red cells large numbers were seen in surrounding lymph spaces. This is not at all conclusive, as similar collections of red cells were found in the lymph spaces surrounding nodes whose sinuses showed no characteristics of hæmolymph nodes. In several cases nodes containing red cells were observed in which afferent lymphatics were filled more or less completely with red cells. In these the appearances of a hæmolymph node were present, yet there was distinct proof that red cells were being brought by lymph vessels. An example is shown in the accompanying figure.



Lymph node, showing red blood cells in sinuses and in afterent lymphatic.

This is reproduced from a photomicrograph of an axillary node removed during an amputation of the breast for carcinoma. In this case there was obviously extravasation of blood in the region whose lymphatics were tributary to the node. Several other such instances were found. The fact that in some instances red cells are brought to a node by afferent lymphatics does not prove that this is the invariable explanation of their presence. In a red deer examined a few minutes after death, immediately following a wound with comminution of the pelvic bones and extensive laceration of the adjacent soft parts, large numbers of small dark-red nodes were

found in the prevertebral region of the abdomen and thorax and along the renal vessels. The peripheral and central sinuses of these nodes contained many red cells but no evidence of recent or former phagocytosis, while in places where the sinuses were completely filled with red eells the adjacent lymphoid tissue was also so densely packed with red eells as to suggest a local hemorrhage. The bloodvessels of the nodes were greatly eongested. There were no hemorrhages in the neighboring tissues. While these nodes were so extensively distributed as to suggest that local extravasation of blood eould not have been responsible for their appearance, the complete absence of phagoeytosis in all examined would suggest that the red cells had entered the sinuses only shortly before fixation of the tissues. The presence of hemorrhages in the lymphoid tissue would also favor the view that these were ordinary lymph nodes with recent hemorrhages into the lymphoid tissue and thence into the sinuses, eaused probably by great disturbance of the circulatory system incident to the traumatism and shock.

With a view to determining the possible influence of circulatory disturbances in producing appearances which might be described as hæmolymph nodes, the following experiment was carried out: A rabbit was anæsthetized with ether and the inferior vena cava ligated in two places, just above and below the left renal vein. The animal was found dead in the morning, about twenty hours later. Viscera normal, except great congestion of the left kidney and spleen. In contrast to the negative results obtained in previous examinations for nodes containing red cells in normal rabbits, red corpuscles were

discovered in six of the nodes studied.

That circulatory disturbanees will not, however, always cause the presence of red cells in lymph nodes was demonstrated by two other experiments upon rabbits. In one, ether anæsthesia, ligation of aorta, inferior vena cava, and right ureter en masse. Rabbit found dead next morning. Viscera normal, except congestion of kidney and desquamation of eells of its tubules. In spite of the intense eireulatory disturbances, red cells were found in the sinuses of only three of eleven nodes, and of the positive specimens one showed hemorrhages into the lymphoid tissue and blood in adjacent lymph spaces. In another rabbit: ligation of the right femoral vessels after bleeding from the artery, under ether anæsthesia, repeating this eighteen days later with the left femoral vessels, and killing a day later by severing the medulla. General anæmia; cheesy area surrounded by consolidation in lung; other viscera practically Nodes from the immediate vicinity of the former and recent operations showed no red cells in their sinuses. In one mesenterie node they were found enclosed in phagoeytes; in two others pigment masses were observed in such cells.

Hemolymph nodes were found in cases in which there was no

hyperæmia.

These observations would seem to show that circulatory disturbances may cause the pressure of red cells in sinuses of nodes, but are not sufficient to account for their appearance in most cases.

That the presence of red cells in the sinuses may be caused by toxic substances within the body was shown by subcutaneous injection of ricin into a normal dog. In all of twenty-one nodes from the cervical, axillary, bronchial, retrosternal, gastric, mesenteric, retroperitoneal, and pelvic regions many red cells were found in the sinuses and in adjacent lymph spaces, with marked congestion of bloodvessels. Similar results, with marked endothelial hyperplasia in the sinuses, were obtained by ricin injection into a rabbit. While these experiments demonstrate that a poison in the circulation may induce the presence of red cells in the sinuses of lymph nodes the toxic action was too severe to draw strict inferences in regard to the behavior of nodes under comparatively normal circumstances.

In three dogs examined, into the peritoneal cavities of which 1 per cent. solution of zinc chloride had been injected for experimental purposes, the abdominal cavities were found post-mortem to contain bloody exudate. In one animal red cells were found in the sinuses of eleven out of fifteen mesenteric and prevertebral nodes; in a second dog, red cells in sinuses of six out of eight nodes from the anterior mediastinum; in the third, red cells or their remains free or in phagocytes in all but two of twenty-seven nodes from the prevertebral, renal, mesenteric and auterior mediastinal regions. some cases the adjacent lymph spaces contained red cells. red corpuscles in these nodes were evidently brought by afferent lymphatics, although none of the sections studied showed their entrance, since at various points in their circumference the peripheral sinuses were closely packed with red cells, and communicating portions of the sinuses contained phagocytes filled with red cells and some red cells free, while toward the centre of the node phagocytosis was just beginning, and since adjacent lymph spaces were filled with red cells. It is unlikely that all of the nodes containing red cells were hemolymph nodes. Probably many were lymph nodes whose endothelium was exerting phagocytic powers in response to stimulation by the toxic substance, zinc chloride, or by some substance produced by its action, perhaps by damaged red cells from the peritoneal cavity. The occurrence of red cells in many of the nodes in these cases may, therefore, have been due to absorption of extravasated blood or to the presence of a toxic substance in the blood. That the presence of toxins does not necessarily cause phagocytic destruction of red cells in the sinuses was shown by negative findings in two rabbits. One of these had been injected with the toxin of the bacillus of rabbit septicæmia (Lartigau); the other had been subjected to the influence of the toxin of tubercle bacilli.

To summarize: absorption of extravasated blood, circulatory disturbances, and toxic substances in the circulation may cause the appearance of red cells in the sinuses of lymph nodes, but there are many nodes in which this explanation is unsatisfactory.

# II. Evidence in Favor of Interpretation of "Hæmolymph Nodes" as Organs Sui Generis.

1. Constant Occurrence. The constant occurrence of hæmolymph nodes in the dog was shown by the following experiments: Four dogs were instantly killed by dividing the medulla, two of these subsequently being found to have microscopically normal viscera, two chronic diffuse nephritis and associated cardiac lesions; one by bleeding while chloroformed, viscera microscopically normal; one by chloroform alone; three by intravenous injections of staining fluid or pigment in suspension, viscera normal, except congestion. In each of three cases a number of hæmolymph nodes were found. The occurrence of all stages of phagocytic destruction of red cells in the sinuses in normal animals killed without unnecessary traumatism, and the nodes of which were hardened within a few minutes after death, shows that this presence of red cells in the sinuses and this blood destruction were not the result of the manipulations or a pathological condition but evidence of the performance of a normal function of the nodes. In one guinea-pig killed by chloroform a hæmolymph node was found, showing red cell destruction by phagocytes. In two of three cats examined after killing with chloroform nodes were obtained, the sinuses of which contained red cells free and in phagocytes. Although red cells were found in lymph spaces in fat surrounding the nodes, there was no reason for attributing the presence of red cells in the sinuses to pathological conditions caused by killing with chloroform, or by rupture of bloodvessels while struggling, since some of these cells were already within phagocytes. In three normal rabbits, two with cholecystitis from bacterial injection, two injected with bacterial toxines, and one splenectomized and subsequently immunized to bullock's blood, red cells were not found in the sinuses, though others have detected them in rabbits, but pigment masses were observed in some phagocytes in sinuses. In human subjects nodes containing red cells were discovered in such varied cases as infants dying from asphyxia neonatorum, gastroenteritis, status lymphaticus, and cerebral hemorrhage after forceps delivery; adults, from pneumonia, pulmonary and laryngeal tuberculosis and splenic anæmia. In a number of autopsy cases in which but few nodes were studied hæmolymph nodes were not found.

2. Intimate Association with Ordinary Lymph Nodes. The nodes whose sinuses contain red cells are often closely connected with ordinary lymph nodes. In one normal dog examined two nodes

were found so closely approximated as to be separated by only a few connective-tissue fibres, except at the point where blood and lymph vessels were situated. The circulatory relations could not be exactly determined. One was a typical lymph node with fine reticulum and no red cells in its sinuses; the other possessed a coarser reticulum and its sinuses contained many red cells. The two nodes were so closely connected that if the presence in the blood of some substance stimulating lymph nodes to accomplish the destruction of red blood cells was the cause of the one assuming the appearance described as that of a hæmolymph node, it would seem certain that the same influence would have acted upon the other node. On the contrary, the general appearance of the two nodes was so different and the distribution of red cells in one so distinctly marked that it would appear there was a fundamental difference in their structure and circulatory connections.

3. Circulatory Relations. The most direct evidence of the existence of hæmolyph nodes as organs sui generis would seem to be the demonstration of bloodvessels directly entering the sinuses, though it is possible that diapedesis may be responsible in some cases for the presence of red cells in them. In both dog and man I have been able to discover what appeared to be direct termination of a capillary in a sinus, but the possibility of artefacts in so delicate a tissue as a capillary wall or the lining of a sinus makes such ocular evidence unreliable. Many hæmolymph nodes appear to bc more vascular than lymph nodes. The interstitial injections which have been employed by others seem unreliable, as the needle may pass into either a lymph or a blood sinus, or both, so that both systems may be injected, rendering differentiation uncertain. Two attempts to make a physiological injection of dogs through the femoral vein failed, one because the insoluble substance suspended caused embolism, the other because of the diffusibility of the material employed. In a third case insoluble Berlin blue suspended in normal salt solution warmed to body temperature was slowly injected into the proximal stump of a divided femoral vein of an anæsthetized dog, while bleeding was permitted from the distal stump in order to prevent undue increase of blood pressure. After ten or fifteen minutes of such injection the animal died. pericardial, thoracic, and abdominal cavities were at once injected with 5 per cent. formaldehyde solution to fix the tissue cells, and the body placed in cold storage for thirty-six hours. All organs normal. In twelve of twenty-five nodes examined red cells were discovered in the sinuses. In only three was the Berlin blue found in the sinuses with the red cells, but in these three at least the coincident presence in sinuses of the recently injected pigment, together with fresh red cells not in phagocytes, would strongly point to a direct communication between the circulatory system and the sinuses of the nodes.

4. Histological Differentiation. The greater coarseness of the reticulum of hæmolymph nodes as compared with that of lymph nodes has been confirmed by the present study, as has the lack of differentiation between cortical and medullary regions in typical hæmolymph nodes. The frequent presence of mast cells and also of eosinophiles has been noted. The eosinophiles seem most frequent in hæmolymph nodes and in lymph nodes in cases with extreme hæmolysis such as splenic anæmia. This suggests an association between the eosinophilic granules and the destroyed red cells. Warthin's statement that phagocytes containing red and white cells are found in all sinuses of hæmolymph nodes, while in lymph nodes they are usually confined to the medullary portion, appears to be borne out.

While having no positive evidence to present in favor of the belief that transformation of fat lobules into hæmolymph or lymph nodes, or of the latter into each other, occurs, the writer has observed,

in several instances, appearances which favor this view.

5. Functions. No evidence of red cell formation could be found. The chief function is obviously destruction of red blood cells; others are formation of leukocytes, their destruction by phagocytes, and probably formation of blood plasma. They may also be concerned in the production of eosinophiles and of phagocytes for the general circulation.

That destruction of red blood cells is an intermittently exercised function and often a purely local process, not due to hæmolytic substances in the general circulation, is shown by the occurrence simultaneously in different nodes or in different parts of the same node of its various stages. These stages are: red cells free in sinuses; apparently adherent to the periphery of the phagocytes; unchanged but contained in enlarged phagocytes; red cells disintegrating within phagocytes which are now stained more deeply red by eosin; red cells not seen, phagocytes deep reddish-yellow; phagocytes smaller, staining normally, containing granules or globules of brownish-yellow pigment; phagocytes of normal size, pigment free in sinuses.

In a node physiologically injected with Berlin blue, for example, one portion of the sinuses contained red cells which had entered long enough before to have been nearly destroyed by phagocytes, while in another portion were fresh red cells which had entered with the injected pigment immediately before death. In explanation of this intermittent action it seems most logical to believe that in some cases the bloodvessels bringing the red cells become blocked temporarily by the mass of red cells and enlarged and proliferated phagocytes in the sinuses. Blood pressure in the node is probably an important factor. In other cases the intermittent action is difficult to explain, but it may be due in some to the presence of hemolytic substances in the blood plasma. These might cause

changes in either blood cells or vessel walls which would lead to

diapedesis into the sinuses.

Conclusions. Both histological and experimental evidence is strongly indicative of the existence of the hæmolymph node as an organ sui generis. In the light of our present knowledge the chief practical point, however, is to recognize the capability for phagocytic destruction of red blood cells which is possessed to a high degree by certain lymphoid structures, rather than to dwell upon the individuality of the hæmolymph node. The occurrence of transition forms from the node containing blood sinuses only to that with sinuses containing lymph alone renders a strict classification impossible. For practical purposes Warthin's grouping of all varieties under the heading of hæmolymph nodes appears eminently satisfactory.

To Dr. George C. Freeborn I am indebted for many valuable suggestions in connection with this investigation; to Dr. A. J. Lartigau for aid in the operative work, and to Dr. Edward Leaming

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## SYPHILITIC AFFECTIONS OF THE SKIN AND OSSEOUS SYSTEM IN THE NEWBORN.

## By W. REYNOLDS WILSON, M.D., of philadelphia.

SYPHILITIC infection may be transmitted in varying degrees of intensity. Its manifestations follow certain definite rules. Every newborn infant, the victim of transmitted syphilis, may not necessarily exhibit the taint; on the other hand, in the largest number of conceptions occurring in the earlier stages of syphilis transmissible from one or both parents, abortion or premature expulsion of the fetus is liable to result.

The opportunity of infection occurs:

1. In the presence of a coexistent infection in both parents. This usually results in abortion (Baginsky), although Neumann has recorded the birth of healthy infants under such conditions.

2. In the presence of infection of the male parent alone at the time of conception. In this case the infection is transmitted directly to the fetus, and is in reality the result of direct contagion. Although the pregnancy may not be interrupted, the infant mortality is great, the children succumbing in proportion to the primariness of the infection in the parent.

3. In the presence, at the time of conception, of maternal infection alone. As in the case of paternal infection, the infant may escape transmission if the paternal disease has reached its tertiary form.

4. In the presence of maternal infection during gestation. The intensity of the infection in such instances depends upon the degree of postponement of the postconceptional infection in the mother.

According to Fournier, syphilis in the newborn may present direct congenital manifestations or indirect evidences of infection. In the latter case it is spoken of as hereditary syphilis. The lesions in hereditary syphilis may be either precocious or deferred as to the date of

their appearance.

Congenital syphilis in the newborn is marked by signs of an infection the evolution of which has been completed in utero. Should the infant be born alive, it presents localized areas of separation of the epidermis in the form of blebs, accompanied by excoriation. The skin resembles the condition of maceration in stillborn infants. There is also present retrograde bony development (imperfectly expanded thorax, craniotabes, etc.), enlargement of the liver and spleen. Such infants are usually premature.

Hereditary syphilis in its precocious form affects especially the newborn infant. It is marked by snuffles, hoarse cry, pendulous abdomen, splenic and hepatic enlargement, and the characteristic

syphilides.

The subject of hereditary syphilis with deferred manifestations may present at the time of birth a perfectly healthy appearance. More frequently, however, the infants are emaciated, the skin being of a dull yellowish color and the face presenting a characteristic senile expression.

Syphilis in the newborn may be considered in reference to the skin

localization as follows:

1. The pathognomonic form of eruption in early syphilis is that of a pemphigus (Gastou). The lesion may either exist as a congenital manifestation or may make its appearance at the end of the first week of life. The character of the eruption is twofold. It may appear, first, in the form of violet or reddish patches protruding slightly beyond the surface of the skin and surrounded by a zone of moderate hyperæmia. The elevation of the surface affected is due to the displacement of the epidermis by the accumulation of a sanguinolent fluid, which may rapidly change in color to a greenishyellow. The size of a fully-formed vesicle usually equals that of a small pea. The diameter, however, may reach 1 cm. or more in

extent. The border may be circular or polygonal. Rupture of the bleb leaves an ulcerated, uneven base. Recovery takes place by the formation of a brownish crust, the neighboring skin remaining reddened and squamous. Secondly, the syphiloderm may begin as a pustular eruption the lesions of which proceed rapidly to maturation and take on a varioloform appearance. If the pustules ecoalesce, the resulting exfoliation may assume the character of a squamous dermatitis, producing a condition resembling iehthyosis. Syphilitic pemphigus usually attacks the palmar and plantar surfaces, especially in its vesicular form. The pustular form is found most frequently in the region of the buttocks and genitalia. It may, however, show no elective tendency as to location, appearing on any part of the body or face.

Jacquet regards the pempligus of hereditary syphilis in the newborn in the light of a developed form of a papulomacular syphilide, corresponding to that observed usually as a later manifestation. The exuberance of the lesions resulting in the blcb-like development, according to his view, is due to the normal congestion of the skin and

the delicacy of the epithelial layer in the newborn.

2. A further manifestation often met with is the papulocrosive syphiloderm, which makes its appearance in the crevices of the skin, where moisture is apt to be present, as, for instance, in the genitocrural folds, the axilla, the region of the umbilicus, and the interdigital spaces. The efflorescence occurs in the form of small papules of a yellowish-gray color and a diphtheritic surface, accompanied by a local crythema. This usually results in crosion, which attacks the summit of the papules and permits the escape of a thinnish exudation. The crosion extends peripherally rather than in depth.

3. Probably the most frequently observed syphiloderm in hereditary syphilis is that of erythema. The rash begins very much as a simple erythema, attacking the region of the genitalia and nates. however, may not be confined to these points of election, as it frequently makes its appearance on the face, especially on the forehead and body. The eruption may even extend to the scalp. The eruption is apt to spread rapidly, showing a tendency to infiltration, and resulting in the development of small papules, which show, as the result of erosion, a moistened surface. The efflorescence remaining after the disappearance of the acute erythema presents a coppercolored, papular syphilide characteristic of secondary manifestations. Frequently the papules are disposed at the verge of the anus and the commissure of the lips (Van Harlingen). There may be active desquamation resulting in the formation of thick, yellowish erusts, which, in separating, leave a moist, infiltrated base. Syphilitie crythema, when attacking the region of the umbilicus, very often results in an impetiginous rash, which terminates in local desquamation. Complicating the erythema, there is frequently observed a macular and squamous eruption of the palmar and plantar surfaces.

4. Furunculoid lesions attacking the corium, as well as tuberculous eruptions, are not uncommonly found coincidently with the more typical skin manifestations. Gastou calls attention to the existence of a gummatous condition, which exists in the form of deep tumefactions, in the region surrounding the articulations. This condition must not be mistaken for the infiltration due to periarthritic absects. It is not uncommonly seen in instances of fatal congenital syphilis.

As in acquired syphilis, the lesions are apt to be symmetrical and are characterized by polymorphism. Owing to the latter characteristic, it is sometimes difficult to differentiate the varieties in syphilitic erythema, the simple form frequently merging into the squamous

and impetiginous forms.

Paronychia may be mentioned among the syphilides appearing in the newborn. Although the infiltration surrounding the matrix may be extensive, it is not likely to result in ulceration. Fissures occurring at the borders of the mucous membrane are commonly seen, situated in the region of the anus and lips. Fissures in the epidermis of the scrotum, and, in the female, in the region of the fourchette, may be observed.

Mucous Membranes. Syphilis of the mucosæ may appear frequently as the primary manifestation in hereditary transmission. this way the coryza may appear as the initial manifestation. The nasal secretion is at first sanious, becoming afterward greenish and purulent. It is frequently mixed with blood. It is irritating to the adjacent skin and often fetid. The crusts which form from the drying secretions may give rise, through their detachment, to epistaxis. The mucous membrane becomes swollen and the submucosa infiltrated, often to such extent as to interfere with the nasal respiration. The buccal mucous membrane, the tongue, the hard palate may become individually the seat of mucous patches, the sites of which offer local areas of ulceration in the process of cicatrization. The pharynx is usually swollen and reddened. The laryngeal mucous membrane may also partake of the hyperæmia and swelling, causing characteristic hoarseness, and leading often to extinction of the voice. Dyspnœa may sometimes oceur, simulating laryngismus stridulus and resulting rapidly in death by asphyxia. Inflammation of the middle ear, accompanied by otorrhea, is of infrequent occurrence.

The Osseous System. The changes in the osseous system affect the long bones as a rule, less frequently the phalanges. The pathological changes in the eranial bones are usually associated with the evolution of infantile syphilis in its later stages. The bones of the head may present, however, a condition of eraniotabes. Undue protrusion of the parietal eminences with deeply-marked sutures (natiform eranium) may rarely be observed. Microcephalus or hydro-

cephalus may be present in eachectic infants.

The abnormalities occurring in the long bones affect usually the juncture of the diaphysis and epiphysis. In an undeveloped state

the lesion may exist as an osteochondritis, which may offer no external evidence. In acute or progressive form it is marked clinically by an indifferent swelling, which may not be detected beneath the soft tissue; occasionally by a palpable enlargement. The condition may make its appearance soon after birth. If the lesions be multiple and pronounced in development they may present the appearance of pseudosyphilitic infantile paralysis. The clinical picture of this disease is described by Parrot. When the infant in a pronounced case is suspended by the axillæ the extremities hang flaccid. If the skin is pinched the muscles move, but the position of the member is not changed. On the other hand, the infant will suffer without resistance such displacement of its extremities. If the legs are extended while the child is in the dorsal decubitus they will resume their flexed position, but the movement is accompanied by pain. The joints may be tumefied. Crepitation and fluctuation may be present. Such extensive involvement usually results in a fatal outcome. The inflammation and loss of continuity producing the symptoms just described are due, according to Gastou, to a justo-epiphyseal osteitis. The suppuration which is present usually invades the joint and leads uniformly to the destruction of the cartilage and the separation of the epiphysis. The apparent muscular relaxation present in such cases may be confused with paralysis of central origin, due to such causes as intracranial hemorrhage and obstetrical traunatism. may likewise simulate the muscular immotility present in fractures and luxations. The condition is not to be confused with epiphyseal separation due to the destruction of the cartilage, found in the putrefactive invasion of the tissues in macerated infants. In instances of the purulent destruction of the epiphyseal attachment, the presence of streptococcus denotes the possibility of the septic process occurring secondarily to the specific inflammation. The lesion may be found at either end of the femur, at the distal end of the tibia, and the bones of the forearm (Ziegler).

As to the pathology, the site of the lesion is the so-called zone of proliferation—i. e., the transitional cartilaginous area that separates the epiphysis from the shaft of the bone. According to Kassowitz and Heubner, the progress of the condition may be divided into three stages: 1. A premature deposit of the primary calcareous infiltration in the original cartilaginous substance. 2. An irregular invasion by this calcifying process of the area of intermediary cartilage (the area in which the cartilage cells begin to arrange themselves to form the primary cartilaginous trabeculæ), with an overgrowth of the cartilaginous trabeculæ and with the premature deposit of bone. 3. The development of a granulation zone between the epiphysis and apophysis, followed in some instances with the actual secretion

of pus.

Macroscopically the yellowish line of demarcation at the apophysoepiphyseal juncture corresponding to the zone of proliferation, found post-mortem in newborn infants, represents the early stage of the

process just described.

The digital phalanges may be the seat of the bony involvement in congenital and hereditary syphilis. The periosteum and fibrous structure surrounding the bone are usually affected. Secondarily, the skin and subintegumentary tissues become involved. Suppurative changes resulting in ulcerations are usually not to be observed, on account of the readiness with which the specific infiltration yields to treatment. The proximal phalanx is more frequently involved than the distal phalanx. The finger is apt to be swollen at its base, presenting a pyriform appearance with the characteristic discoloration of the skin. Baginsky has observed a bony deformation of the fingers, resulting in syndactylism in a syphilitic child.

## A STUDY OF THE CALORIC NEEDS OF PREMATURE INFANTS.

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VIERORDT and Rubner were the first to investigate the metabolism of the infant. Camerer, in 1889, collected a large amount of material and endeavored to determine in heat units the nutritive needs of infants of various ages. He calculated the caloric contents of breast milk on the basis of Pfeiffer's analyses. A considerable number of observations have been made by different men since that time. Each one has, as a rule, made but one or two. of them have been made on breast-fed infants; a few on artificially fed. Some of them have extended over the first year, but most of them only over short periods of time. Czerny and Keller, in their hand-book published in 1902, have reviewed the work of previous observers in detail and added a considerable amount of material of their own. Since then Beuthner has studied three cases, one of which was fed entirely on breast milk, the others partly on breast milk and partly on artificial food. In 1902 he summed up the cases fed on breast milk hitherto studied in private practice. He included the cases of Ahlfeldt (2), Camerer (4), Feer (3), Hähner (4), Laure (1), Pfeiffer (2), Weigelin (1), Oppenheimer (1), and his own (3). The average number of calories per kilo taken daily was as follows.

1,	week		59 ca	lories.	10 v	veeks		104 calories.		
2	wceks		100	44	14	\$4		96	66	
4	"		106	4.4	17	41		91	+6	
7	**		114	<b>6</b>	20	66		85	11	

In all these experiments the calorie worth of the nourishment was reekoned on the usual basis that 1 gram of albumin equals 4.1 calories, 1 gram of earbohydrates 4.1 calories, and 1 gram of fat 9.3 calories. There must be some doubt, of course, whether these figures, which were ealeulated expressly for the mixed food of a man, can be used in estimating the nutritive value of milk for an infant. In the mixed diet of the adult about 8 per cent. of the total worth is lost in the feees. Czerny and Keller have shown that this loss is much less in healthy children fed on milk. All these observers estimated the caloric value of human milk at 650 calories per litre, and of cow's milk at 670 calories per litre. This standard for the calorie contents of woman's milk is based on an estimated composition. Everyone knows that the milk of different women varies, especially in its fat contents, and that the milk of the same woman varies from day to day and from nursing to nursing. These physiological variations in the composition of woman's milk make an average caloric worth elusory. This average figure is still more elusory when we realize that the accepted calorie value of 650 ealories per litre is based on the average of the analyses of the milk of two women, one of whom had a milk poor in fat, the other a milk rich in fat. Schlossmann, moreover, obtained as the result of 218. analyses of woman's milk an average value of 782 ealories per litre. He used this figure as the basis of his investigations. It is evident that the figures of previous observers will be materially altered if this ealorie value is accepted. It is evident, therefore, that figures based on such an average calorie value per litre of milk cannot be of great value.

Henbner draws the following conclusions from the cases of Feer, Finkelstein, Camerer, and others: An alimentation whose quotient of energy does not exceed 70 ealories is insufficient for an infant, even if breast-fed, to prosper on, at least during the first six months. In order to get a normal gain a quotient of energy of at least 100 calories with natural alimentation and of 120 with artificial alimentation is necessary. After the sixth month a given quotient of energy gives better results as regards gain in weight than in the first six months; that is to say, in the second half of the first year the organism works more economically than at the beginning of life. In order to obtain the same results a larger quotient of energy is required in artificial alimentation than in natural alimentation. He believes that the less favorable results of artificial food are due to the greater work which cow's milk imposes on the digestive This work absorbs a certain number of ealories which normally are made use of by the organism. Other writers have attributed the difference in the results to the difference in the

casein of woman's and cow's milk.

In attempting to determine how much nourishment a healthy suckling needs it is of the greatest importance to determine by what standard the amount of this need is to be measured. In adults under physiological conditions enough nourishment must be taken to keep up the weight. This is not sufficient for infants in the first year, who must take enough nourishment to make possible a gain in body substance. This gain must also be of a certain definite kind. A gain in weight alone is not sufficient and cannot be accepted as a reliable guide to the worth of the food. At present we are not in a position to say what substances and what quantities of these substances are necessary to meet the loss of the body and to make possible a normal gain in development. We do know that the infant must have albumin, but that it can thrive on a comparatively small amount. Whether fat or carbohydrates can be omitted without causing harm to the organism has not yet been determined in the healthy infant. Single observations on sick children point to an affirmative answer.

The number of experiments which have thus far been made in the metabolism of infancy are too small to justify any general and sweeping conclusions. It must be remembered, moreover, that figures based on an average caloric contents of milk show nothing more than does the quantity of the nourishment. A study of the curve of nourishment in healthy infants shows in the beginning for a longer or shorter time a daily increase in the amount of milk taken, which increase, nevertheless, steadily diminishes as the infant becomes older. In the first weeks of life, in breast-fed children, the amount of nourishment taken is about one-fifth of the body weight. It gradually diminishes and from the middle of the first to the middle of the second quarter-year remains between one-sixth and one-seventh, and at the end of the first half-year is about one-eighth of the body weight.

The variations in the rate of development of children who take the same quantity of woman's milk may be largely explained by the differences in the chemical composition of the milk which they receive. Moreover, as the result of the variations in the area of the surface of the body different percentages of the energy taken in are given off in the form of heat. Finally, it is possible that the differences in the composition of the body substance in different children

may play a part.

Czerny and Keller think that the figures which have been obtained by averaging the number of calories taken by the various infants which have been studied are larger than the nutritive need of a healthy infant. One of the infants studied in their clinic shows that Heubner's assumption that an intake of less than 70 calories per kilo, even in breast-fed infants, is not consistent with a normal increase in weight for the first half-year is erroneous. In this case less than 70 calories per kilo were taken for six weeks. The increase in weight was, nevertheless, 15 grams daily. They also give various observations which show that in breast-fed infants less than 100

ealories per kilo is completely sufficient for a satisfactory development.

They do not agree with Heubner's assertion that with an artificial food satisfactory development is impossible on less than 120 calories per kilo daily. Heubner based his opinion on Finkelstein's study of a healthy infant. Another case of Finkelstein's which was also on an artificial food did well and gained regularly on much less than 120 calories per kilo, taking an average of 103.6 calories per kilo in the first quarter-year, 102.5 in the second quarter, and 99 in the third quarter. They consider that the quantity of milk necessary to give 120 calories per kilo of body weight is overfeeding.

They do not agree with Heubner that a larger caloric worth of cow's milk is necessary than of breast milk. They state that metabolism experiments have thrown but little light on the comparative nutritive worth of woman's and cow's milk for healthy infants. (They quote Rubner and Heubner's experiments.) These show no important differences as regards the utilization of the constituents of cow's and woman's milk, the physiological results being almost the same in both cases. They assert that the caloric need of a healthy infant is no greater when nourished on cow's milk than on human milk, and that the assumption that when cow's milk is taken more of the energy ingested is used up by the digestive tract than when breast milk is taken is therefore unwarranted.

It is a well-known fact that small bodies have a greater surface area in proportion to their mass than have large bodies. The loss of heat is therefore relatively greater in proportion to the weight in small than in large bodies. Rubner first recognized the importance of this fact in relation to tissue changes in living animals, and demonstrated that the tissue changes are proportional at every age to the size of the surface of the body. Young individuals, therefore, show a relatively greater destruction of material than older, and hence require relatively larger amounts of nonrishment. This difference in size explains to a certain extent, but not entirely, the far greater number of calories per kilo required by infants than by adults in order to thrive. The rest of the infant's greater requirement is accounted for by the fact that the infant uses up a considerable amount of energy in growth.

Reasoning on the same lines, premature infants, being so small, should require even more ealories per kilo than full-term infants in order to thrive. Heubner compared an artificially-fed premature infant studied by Finkelstein with a breast-fed full-term infant studied by Feer and another artificially-fed full-term infant studied by Finkelstein, and found that it did not do so well as the others. Its gain was only one-half as rapid as that of the artificially-fed infant, although after the sixth week it took as many or more calories per kilo of weight. During the first three weeks it took an average of 25 calories per kilo and made no gain, while in the

two weeks following it took between 50 and 90 calories per kilo and made a slight gain. During the next four weeks it took an average of 104 calories per kilo, and from the tenth to the seventeenth weeks inclusive 135 calories per kilo. It averaged 120 calories per kilo from the eighteenth to the thirty-ninth week inclusive, and 107 calories per kilo from the fortieth to the fifty-second week. During the first quarter of the year it made an average daily gain of 12 grams, in the second one of 18 grams, in the third one of 15 grams, and in the last one of 2 grams. Its initial weight was 1350 grams, while at the end of the year its weight was 5750 grams. It was fed on peptonized milk.

Heubner explains the smaller gain on a relatively equal or greater intake of energy on the principles detailed above. Another possible reason why premature infants might be expected to require a relatively greater intake of energy lies in the comparatively undeveloped condition of the digestive power which results in a less complete utilization of the food ingested. No proof of this latter assumption

is, however, at hand.

Beuthner studied an infant six or seven weeks premature for twenty-five weeks. It was entirely breast-fed for seven weeks, and was then given in addition cow's milk diluted with a cereal decoction to the end of the twenty-fifth week, at which time the observation was discontinued. It weighed 2400 grams at birth and 6800 grams at the end of the twenty-fifth week, having made an average daily gain of 25 grams. During the first quarter it took a daily average of 113.1 calories per kilo, and during the second quarter one of 92.2 calories per kilo.

Schlossmann studied an infant four or five weeks premature from the twelfth to the eightieth day. It was breast-fed. It weighed 2230 grams on the twelfth day and 3310 grams on the eightieth day, having made an average daily gain of 16 grams. It took an average of 119 calories per kilo daily and made an average daily gain of

5.5 grams per kilo.

These cases, as far as they go, confirm Heubner's assumption that premature infants require a relatively greater amount of nourishment than full-term infants, and that a larger number of calories is necessary in a substitute food than in breast milk. The differences are so slight, however, that but little importance can be attached to them.

During the past winter I have studied from the point of view of the quotient of energy the feeding of six premature infants, five of them at the Infants' Hospital and one in private practice. All were feed on modified cow's milk of definite percentages prepared at the Walker-Gordon Laboratory. The composition of the food being known, it was easy to calculate its caloric contents. It is possible that the composition of the food may not always have been exactly what it was supposed to be. Edsall's recent analyses of milk pre-

pared at the Walker-Gordon Laboratory show, however, that these variations must have been very small, certainly not large enough to have vitiated to any extent the value of the results. They certainly must be more accurate than those obtained on the basis of the average analyses of woman's and cow's milk. The amount of food taken at each feeding was carefully measured. The caloric value was calculated on the basis that 1 gram of sugar or proteids equals 4.1 calories, and 1 gram of fat 9.3 calories.

Unfortunately all the babies did not do uninterruptedly well. One died when twenty-seven days old, of a eongenital cardiac lesion complicated by ateleetasis of the lungs. Its digestion had been good from the first, however, and it had shown no signs of its cardiac or pulmonary lesions until its sudden collapse and death. One left the hospital when three weeks old, not gaining, but doing very well in other ways. Two did very well and gained steadily. One gained steadily for ten weeks and another for eight weeks, after which both had more or less disturbance of digestion and did not gain regularly, sometimes gaining and sometimes losing. Most of them showed a tendency to have too many dejections. These were, as a rule, of good color and odor, but were rather loose and contained fine curds. They did not seem to interfere with the gain in weight, but suggested that a portion of the food was not properly utilized. The histories with charts are given in more detail below:

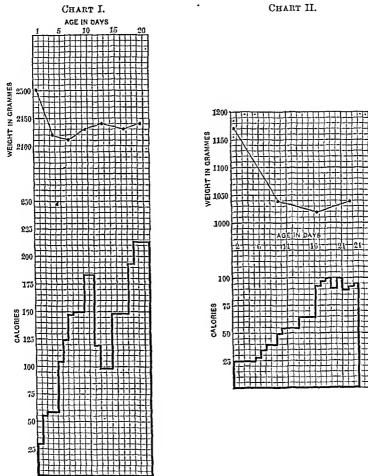
Ruth C. was brought to the Infants' Hospital February 1, 1903, when six hours old. She was thought to be two months premature. The physical examination showed nothing abnormal. Her cry was strong. Her weight was 2500 grams. Her temperature was about normal during the whole of her stay in the hospital. She always took her food well and never vomited. She had from one to four movements daily, usually one or two, which were generally a little green and contained a few eurds. The movements were not as good on February 12th. She was given calomel and her food was cut down for forty-eight hours. She was discharged February 22d at her parents' request. She had been taken out of the incubator and was doing well. Her weight was 2440 grams.

1903, when twenty-four hours old. He was supposed to be two months premature. He was feeble and had a feeble ery. His extremities were cool. The heart sounds were normal, the rate slow. No further examination was made. His weight was 1170 grams. He was at once put in the ineubator. His temperature remained subnormal until May 9th, after which it was irregular, but usually elevated. He took his food well from a Breck feeder, but was not able to take an ordinary nipple. He regurgitated a

James McL. was admitted to the Infants' Hospital April 24,

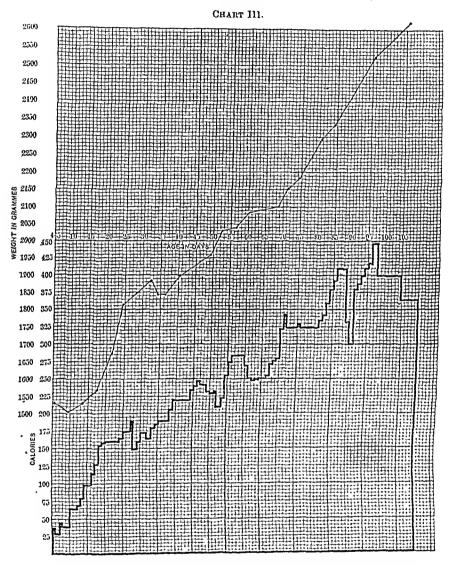
little during the last two or three days. During the first nine days he had one movement daily which, after the meconium was passed, was well digested. After that time he had from two to six move-

ments daily, usually well digested. They were well digested on the day of his death. He seemed to be doing finely until the weather suddenly became hot. He immediately began to fail and died May 20th. His weight on the day of his death was 1040 grams. The autopsy showed that both the foramen ovale and the ductus arteriosus were open and that portions of both lungs had never expanded.



Charles S. was first seen on February 3, 1903 when twelve hours old. He was at least four weeks premature. Physical examination showed nothing abnormal. He acted fairly vigorously and had a strong cry. His weight was 1530 grams. He was put in a padded crib. When five days old he suddenly collapsed and almost died. After this he was feeble for a considerable time. At first he had to be fed with a Breck feeder and sometimes with a dropper. He usually took his food fairly well, but showed a tendency to spit it up if he were at all overfed. The food supply had to be cut down several times temporarily on this account. There was a slight tendency

to constipation, but the movements were, as a rule, well digested. He had a good deal of colic. The observation was stopped on May 19th, when he was fifteen weeks old, because the family were going into the country for the summer, where they had to use a home modification of milk. His weight at that time was 2620

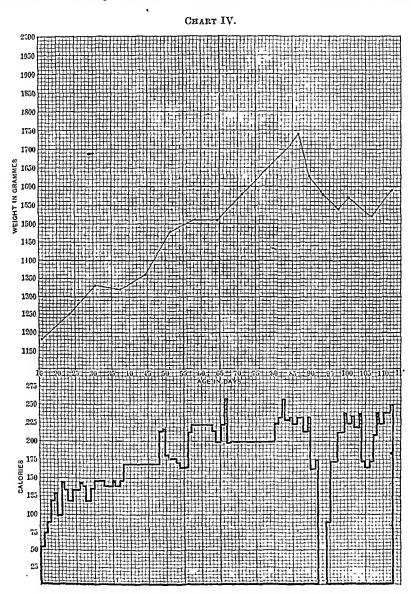


grams, making an average daily gain of a little over 10 grams. He was doing well at that time and has continued to do so.

Pauline J. was admitted to the Infants' Hospital March 20, 1903 when two weeks old. She was born at the Lying-in Hospital

1903, when two weeks old. She was born at the Lying-in Hospital and had been in an incubator there before she came to the Infants' Hospital. She was supposed to have been about two months

premature. She was small, emaciated, and markedly jauudiced. The fontanelle was depressed, and the cranial bones overlapped. The physical examination showed nothing else abnormal. Her cry was strong. Her weight was 1180 grams. She was kept in an incubator until April 25th, and would have been kept there longer



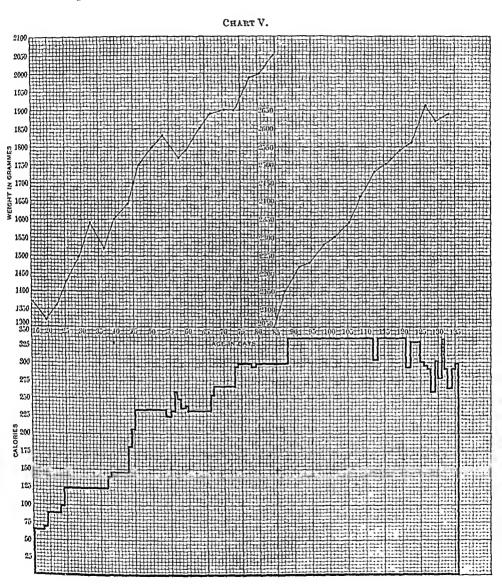
if the incubator had not been needed for another baby. She was kept in a padded crib until the middle of June. She was first bathed and dressed May 18th. Her temperature was usually normal or a little above normal. She was fed partly with a dropper and partly with a Breck feeder until March 24th, then with a Breck feeder until April 23d, after which she took the nipple. She usually

took her food fairly well. She did not vomit at all until about the second week in May, after which she at times vomited a good deal and at others not at all. On this account the food supply had to be cut down on several occasions and at one time milk was omitted entirely. After May 1st there was a slight tendency to looseness of the bowels. At times she had as many as seven or eight in twenty-four hours. These were either yellowish or yellowish-green, with fine curds and occasionally a little mucus. The movements, however, on the whole, were not bad. They certainly did not interfere with her general condition or prevent her from gaining until June 1st, when she was twelve weeks old. She then weighed 1720 grams, having made an average daily gain of 8 grams. She did not do as well after the hot weather began in June, although she developed no new symptoms, did not vomit any more or have a greater number of movements. She was discharged June 29th, when sixteen and one-half weeks old, because the hospital was closing for the summer. At that time she was not doing very well, was having many movements and vomiting a little. Her weight was 1600 grams. She was evidently sick after June 1st, and hence her records from this date on can hardly be properly used in estimating the caloric need of a normal infant.

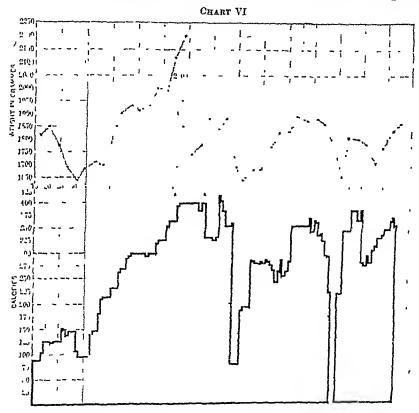
Emanuel B. was admitted to the Infants' Hospital January 17, 1903, when two weeks old. He was supposed to be about two months premature. He had spent the first two weeks in an incubator at the Lying-in Hospital. While there he vomited every few days and was constipated. The physical examination showed nothing abnormal. His weight was 1370 grams. He was put in a padded crib, dressed March 5th, bathed March 23d and taken out of the padded crib April 26th. His temperature was subnormal during the first two weeks, but after that was normal. He always took his food well and very seldom vomited, at one time not for ten weeks. He had from two to five movements daily, which were usually yellow but sometimes green, and often contained small curds and sometimes a little mucus. On the whole the movements were mostly satisfactory except that they were increased in number. He was doing fairly well when he left the hospital, May 19th. He was then nineteen weeks old and weighed 2640 grams. He had had a little fever, had not taken his food quite as well, and had not gained during his last ten days in the hospital. Nothing definitely wrong was made out, however. It is hardly fair, nevertheless, to consider him a well baby after May 9th. The last ten days should not be counted in drawing conclusions. From the fifteenth to the one hundred and twenty-fifth day he made an average daily gain of a little over 12 grams.

James J. was admitted to the Infants' Hospital January 22, 1903, when fourteen days old. He was supposed to have been one month premature. He spent the first two weeks in the Lying-in

Hospital. He was thin and the anterior fontanelle was somewhat depressed. The physical examination was otherwise negative. His weight was 1820 grams. He was put in a padded crib. He had to be fed with a Breck feeder until March 10th. He was bathed March 13th and taken out of the padded crib April 26th. His temperature was subnormal for nearly a month, after which it



was usually about normal. He was never vigorous and never took his food very well. He did not vomit until the middle of May, after which he vomited occasionally. He had from two to four movements daily up to about the middle of March, after which he had too many movements, often as many as six or eight in twentyfour hours. After April 1st, when he weighed 2430 grams, any attempt to increase the amount or strength of the food caused an increase in the number of movements. These movements were yellowish, or yellowish-green, and contained fine curds. On several occasions the food had to be cut down decidedly, and once milk was entirely omitted. During the last five weeks he had a sore mouth and tongue from time to time. He was much depressed by the first hot weather, which occurred in the middle of May. It was at that time that the milk had to be stopped. He never did as well afterward. He was discharged June 18th in fair condition and gained



in weight. His mouth was well. He was taking his food rather better, was vomiting about once a day and having from three to four movements daily, some of which were normal and some of were green and contained curds. His weight was 2410 grams. The only period in which he did almost uninterruptedly well was from the thirty-second to the eighty-third day. During this time he made an average daily gain of more than 15 grams. His subsequent record is of chief interest in showing the rapid fall in weight when the nourishment was cut down, with a correspondingly rapid rise when it was again increased. It is worthy of study in this connection.

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Age in days.	Grossman.	McLeod.	Stone.	Jeffrey.	Blafkie.	Joyce.	Grossman,	McLeod.	Stone.	Jeffrey.	Blaikie.	Joyce.	Number of cases.	Daily average calories per kilo.
1-5 5-10 10-15 15-20 20-25 25-30 30-35 85-40 40-45 60-65 65-70 70-75 75-80 80-85 85-90 90-95 90-95 90-95 100-105 115-120 120-125 135-140 140-145 145-150 150-155 165-160	61.7 53.5	20. 5 34. 5 56. 7 85. 4 72. 1	33.6 59.0 94.4 95.1 90.8 98.5 114.9 121.0 119.4 123.4 123.4 123.4 133.9 151.0 145.9 161.3 152.6 165.0 160.4 148.4		52.7 72 5 87.2 82.8 86.9 101 5 135.0 129.0 137.2 145.5 152.4 157.2 148.5 149.9 140.7 133.7 124.4 110.6 111.4	55.2 70.3 83.3 72.4 75.2 120.0 132.0 152.3 156.6 170.3 180.6 176.2 156.5 149.5 131.7 64.8 117.1 124.0 112.1 135.5 146.0 145.5  158.7 158.7 158.7 158.7	lost even even even even	lost lost even even even	lost 6.5 14.8 17.0 4.3 10st 7.6 3.1 7.0 2.9 3.8 even 6.6 6.4 8.0 5.1 7.44 3.9 3.0	6.6 8.0 9.3 even 1.5 4.5 12.8 5.4 2.6 even 7.7 6.3 6.0 6.5 lost even lost	lost 13.1 12.3 6.5	2.2 lost lost 2.4 2.3 11.4 11.8 even lost lost 1.8 8.7 4.2 4.1 even lost 7.0 5.9	2336 5 444444444 2222 1111	22.6 43.3 56.4 73.5 82.2 91.3 90.7 98.5 117.2 130.2 131.1 141.5 150.8 149.2 149.2 149.2 149.2 149.2 149.3 161.8 161.8 163.7 138.7 124.4

Further analysis of this table shows that these cases took from the fifteenth to the ninetieth day, that is, during the first quarter after the first two weeks, a daily average of 122.7 calories per kilo of weight, and that from the ninetieth to the one hundred and twenty-fifth day, that is, during the early part of the second quarter, a daily average of 142.9 calories per kilo of weight.

In the first few weeks these infants took less than the average given in Beuthner's table. As they did not gain at first it is probable, however, that in order to avoid upsetting the digestion they were somewhat underfed. These figures justify Heubner's assertions that not less than 70 calories per kilo are necessary during the first six months, and that with artificial alimentation at least 120 calories per kilo are necessary to get a normal gain. They correspond fairly closely with the results obtained by other observers in premature infants during the first three months, Beuthner's infant having averaged 113.1 calories per kilo, Schlossmann's 119 calories per kilo, and Finkelstein's 120 to 135 calories per kilo. In contradistinction to other figures they show a progressive increase in the quotient of energy toward the end of the first quarter and at the beginning of the second quarter. In spite of the high quotient of energy these.

infants did not gain as rapidly as the average normal full-term infant, thus confirming Heubner's assumption that premature infants require a relatively greater amount of nourishment than do full-term infants.

It is very difficult to draw any very satisfactory conclusions from these figures. In some instances when two babies of the same age were taking almost exactly the same relative amount of nourishment one gained and the other lost. In other instances the baby taking the smaller amount of nourishment gained while the other lost. For example, between the fifteenth and twentieth days baby J. gained on 55.2 calories per kilo, while baby B. lost on 52.7 calories per kilo. Between the twentieth and twenty-fifth days baby B. made a large gain on 72.5 calories per kilo, while baby McL. just held his weight on 72.1 calories per kilo and baby J. lost on 70.3 calories. Between the thirtieth and thirty-fifth days baby J. gained on 72.4 calories, while baby S. lost on 98.5 calories. Between the fifty-fifth and sixtieth days babies S. and J. gained on 133.9 calories and 138.6 calories respectively, while baby B. lost on 137.2 calories

In some cases in which two babies of the same age were taking practically the same relative amounts of nourishment, one gained two or three times as much as the other; for example, between the fortieth and forty-fifth days baby J. took a daily average of 120 calories per kilo and made a daily gain of 11.4 grams per kilo, while baby S. took 121 calories and gained only 3.1 grams per kilo.

Again, babies of the same age gained essentially the same amounts on widely differing amounts of nourishment; for example, between the seventieth and seventy-fifth days baby S. made an average daily gain of 6.4 grams per kilo on 151 calories per kilo, while baby J.

gained 6.3 grams on 126.1 calories.

In other instances one baby did better than another for a time, and then a little later the second baby did better than the first; for example, between the twentieth and twenty-fifth days baby B. took 72.5 calories per kilo and gained 13.1 grams per kilo daily, while baby J. lost weight on 70.3 calories. Between the forty-fifth and fiftieth days baby B. took 135 calories per kilo and made a daily gain of 11.4 grams per kilo, while baby J. took 132 calories and gained 11.8 grams. Between the eightieth and eighty-fifth days baby B. took 157.2 calories and gained 6.2 grams, while baby J. took 156.5 calories and gained 8.4 grams.

Again, the same baby did not gain in proportion to the amount of food taken; for example, baby J., between the fortieth and forty-fifth days, took an average of 120 calories per kilo and made an average daily gain of 11.4 grams per kilo; between the forty-fifth and fiftieth days he took 132 calories and gained 11.8 grams; between the fiftieth and fifty-fifth days, 152.3 calories with no gain; between the fifty-fifth and sixtieth days, 156.2 calories with a gain of 2 grams; between the sixtieth and sixty-fifth days, 158.6 calories

with a gain of 6.1 grams; between the sixty-fifth and seventieth days, 170.3 calories with a gain of 12.6 grams, and between the seventieth and seventy-fifth days, 180.6 calories with a gain of 9.2 grams.

The only conclusion which it seems possible to draw from these contradictory figures is that the gain seemed to depend as much, or more, on the digestion and metabolism of the given baby at the given age as on the amount of the food, the age of the baby, or any inherent differences in the individual babies.

Conclusion. The conclusion seems justified from these figures that the caloric need of premature infants is relatively greater than that of full-term infants. This greater need is due in part to the small size and comparatively large surface area of premature infants, which cause them to lose heat faster than do larger, full-term infants, and partly to the incomplete development of their digestive powers, on account of which they utilize a relatively smaller proportion of the caloric value of the food ingested. This conclusion emphasizes the importance of protecting premature infants against loss of heat and of providing for them a food which will throw the least work on the partially developed digestive powers.

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## AN EXPERIMENTAL STUDY OF THE RELATION OF CELLS WITH EOSINOPHILE GRANULATION TO INFECTION WITH AN ANIMAL PARA-SITE (TRICHINA SPIRALIS).

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THE present study has been undertaken in order to determine how the eosinophile leukocytes react when subjected to influences which increase their number in the blood or elsewhere. The leukocytosis which follows infection with bacteria on the one hand has been carefully investigated. Leukocytosis caused by infection with a variety of parasites belonging to the animal kingdom, it is well known, is characterized by an increase of the eosinophile leukocytes; the conditions which influence this phenomenon, on the contrary, are incompletely understood.

<sup>&</sup>lt;sup>1</sup> The present investigation has been conducted with the aid of a grant from the Rockefeller Institute for Medical Research.

Müller and Reider,1 studying the blood of patients suffering with a variety of diseases, found in an individual infected with uneinaria duodenalis that the cosinophile leukocytes constituted 9.6 per cent. of the total number of leukocytes. In a similar case Zappert2 noted a proportion of 17 per cent., and, at the same time, observed Charcot-Leyden crystals in the feces. Bucklers' directed his attention to a variety of parasitic infections and found a considerable increase of the eosinophile cells in association with uncinaria duodenalis, strongyloides intestinalis, and even with such relatively harmless forms as ascaris lumbricoides, tenia solium, aud tænia saginata. In one case of uneinariasis or ankylostomiasis eosinophile cells formed 53.6 per cent. of the white corpuscles, while the total number of leukocytes was 20,600 in one cubic millimetre of blood; infection with ascaris lumbricoides caused eosinophilia of 10 per cent.; infection with both ascaris lumbricoides and oxyuris vermicularis 19.3 per cent. In a fatal case of infection with uncinaria duodenalis Strong found the mucosa, the museularis mucosæ, and the submucosa of the small intestine infiltrated with eosinophile cells. In a similar case described by Yates the same local accumulation was noted, and in the basal part of the mucosa eosinophile cells were so numerous that seventyfive were counted in one field of the oil immersion lens (obj. 1-12th).

To the list of animal parasites causing eosinophilia may be added triehina spiralis (Brown<sup>6</sup>), filaria banerofti (Calvert,<sup>7</sup> Gulland<sup>8</sup>), and bilharzia hæmatobia (Coles<sup>9</sup>). The studies of T. R. Brown and of others who have confirmed his observations have shown that eosinophilia is so constantly associated with trichinosis that its presence may serve as an important factor in the diagnosis of the disease. In the blood of a patient in whose museles Brown subsequently demonstrated triebinæ eosinophile cells constituted, on admission to the Johns Hopkins Hospital, 37 per cent. of the total number of leukocytes. The proportion was somewhat diminished for a time, but subsequently rose and on the fiftieth day after admission reached 68.2 per cent. The total number of leukoeytes varied during the greater part of the illness from 15,000 to 30,000 per cubic millimetre. In specimens of muscle removed at a period preceding the maximum eosinophilia extensive degenerative changes had resulted from the presence of embryonic trichine, and in the altered tissue eosinophile cells with polymorphous nuclei had accumulated in large numbers. Similar phenomena were exhibited by subsequent eases.

Deutsches Arch. f. klin. Med., 1891, vol. xlvill. p. 96.

<sup>&</sup>lt;sup>2</sup> Zeitsch. f. klin. Med., 1893, vol. xxiii. p. 227. Munch. med. Woch., 1894, vol. xli. p. 23.

<sup>4</sup> Circulars on Tropical Diseases, No. 1, Chief Surgeon's Office, Manila, 1901.

<sup>&</sup>lt;sup>5</sup> Bulletin of the Johns Hopkins Hospital, 1901, vol. xil. p. 356.

Journal of Experimental Medicine, 1898, vol. lii. p. 315.

<sup>7</sup> Bulletin of the Johns Hopkins Hospital, 1902, vol. xiil. p. 133.

<sup>8</sup> British Medical Journal, 1902, vol. i. p. 831.

<sup>9</sup> Ibid., p. 1137.

H. U. Williams and Bentz¹ have digested trichinous pork for forty-eight hours at 36° C., with artificial gastric juice containing pepsin and 0.2 per cent. of hydrochloric acid, and have introduced the dried residue into dogs, cats, and frogs. In a considerable proportion of these experiments eosinophile leukocytes in large numbers have collected about it. The phenomenon, as Williams and Bentz state, is probably due to some substance derived from the bodies of the worms, but the experiments, they think, do not entirely exclude the possibility that the result may be due to the action of hydrochloric acid and pepsin or to the agency of bacteria.

The foregoing has shown that a considerable number of diverse animal parasites cause an increase of the eosinophile cells in the general circulation and in several instances a local accumulation in the neighborhood of the parasite. It is not improbable that the parasite secretes some product which has a specific influence upon the eosinophile cells, causing their multiplication. Should it be possible to produce a similar condition experimentally, we would have a ready means of studying the somewhat obscure activities of these cells. It is, moreover, of considerable importance to determine if the eosinophile cells of man and of the lower mammals bear a similar relation to entozoan infection. Study of conditions under which the eosinophile leukocytes are increased in number offers the readiest means of determining their much disputed origin and seat of multiplication.

Calamida<sup>2</sup> has prepared from the tapeworms of the dog, tænia cucumerina and tænia coenurus, an extract which he claims exerts

a chemotactic influence upon the eosinophile cells.

The parasites, previously washed in sterile salt solution, are rubbed with ground glass in a mortar and at the same time treated with salt solution. By means of a Berkefeld filter is obtained a filtrate which, eoncentrated by evaporation, produces death when injected into rabbits and guinea-pigs. This material is hæmolytic for the red blood corpuscles of the rabbit and of the guinea-pig and, injected into the circulation, rapidly causes fatty degeneration of the liver. If a capillary tube containing the fluid is placed in the subcutaneous tissue of the rabbit, at the end of twenty-four hours it will be found to contain leukocytes, of which the greater number are eosinophile cells. Injected into the eirculation, Calamida states, leukocytosis results in six to eight hours, eosinophile cells being increased in greater degree than other forms.

Methods. Hoping to obtain a substance by which the eosinophile leukocytes might be increased at will, I have employed an extract prepared by grinding in a mortar with sand and normal salt solution the body of tænia saginata, first washed with sterile salt solution. By passing the extract through a Pasteur filter a clear yellow fluid

Transactions of the Association of American Physicians, 1903, vol. xviii. p. 152.
 Cent. f. Bakt. und Par., 1901, vol. xxx. p. 374.

is obtained. This filtrate injected into the subcutaneous tissue of guinea-pigs, as much as 10 c.c. being used, failed to produce a noteworthy increase of the eosinophile cells. In one instance their number rose from 1 per cent. to 5 per cent. on the fourth day; in another, from 1.3 per cent. to 5.8 per cent. on the fifth day. The results were somewhat inconstant and, fresh tæniæ being difficult to obtain, this method of increasing the eosinophile cells was discarded.

Since many lower mammals are readily infected with triching, the observations of T. R. Brown upon human infection suggests the possibility of increasing the eosinophile lenkocytes experimentally by this means. H. U. Williams and Bentz, however, found no noteworthy increase of the eosinophile cells in the blood

of rats and cats artificially infected with trichinæ.

For the purpose of the experiments to follow, the guinea-pig has proved convenient. The methods of obtaining the blood and of counting the leukocytes have been described in a previous paper.¹ In any experimental study of the eosinophile cells in the guinea-pig variations in the normal proportion of these cells must obviously be taken into consideration. These variations have been described in the article just cited. A slight increase of eosinophile leukocytes might give uncertain evidence of the results of infection, yet when examinations, continued from day to day, show that their number exhibits characteristic changes, little opportunity for doubt remains. The charts to follow will show that trichinosis in these animals has an effect upon the eosinophile cells which is similar to that observed in man, even though the details of the process are not always the same.

It soon became evident that the severity of the infection exerts an important influence upon the reaction exhibited by the blood, and hence it has been essential to adopt some means by which this factor may be estimated. By the following method the number of triclinæ fed to a given animal is determined with approximate accuracy. A small piece of trichinous pork measuring hardly more than 4 em. in length and half as much across the fibres is freed as far as possible from fat and fascia. The infected pork used in these experiments was obtained from the United States Bureau of Animal Industry through the courtesy of Dr. D. E. Salmon, to whom I desire to express my obligation. From various parts of the meat selected small masses are removed and adjusted to a weight of 0.05 gram. When this particle is teased in glycerin containing 5 per cent. of acetic acid and pressed between two glass slides the number of encapsulated trichine can be conveniently counted with low magnification. From an average of five such counts it is possible to determine how much ment contains a given number of trichine, and though the eysts are not evenly distributed, the following figures will show that an approxi-

<sup>&</sup>lt;sup>1</sup> The American Journal of the Medical Sciences, February, 1904, p. 217.

mate estimate of their number can be made if a small piece of muscle is used:

Specimen	of pork l	No. 1.	Number	of trichin	æ in	0.05 grm			124
• "	**	**	**	"		**			91
44	"	**	**	**		4.8			113
**	**	**	"	**		**			100
44	"	44	**	"		66			128
	•		Mean						111.2
Specimen	of pork l	No. 2.	Number	of triehin	æin	0.05 grm			40
- 44	44	**	45	**		8.6			63
"	61	**	44	**		**			71
**	**		44	14		"			54
. "	"	"	**	64		44	•	•	74
			Mean						60.4
Specimen	of pork	No. 3.	Number	of trichin	æ in	0.05 grm			121
44	"	**	44	46		64			155
44	**	4.6	64	**		46			120
44	16	**	**	**		41			117
"	"	**	4	"		"			103
			Mean						123.2

Increase of Eosinophile Leukocytes with Mild Trichinosis. Pork containing 2000 to 3000 trichinæ fails to cause death or does so only after several weeks. A larger dose is usually fatal within a week or ten days. The milder infection, which will be first considered, is accompanied by characteristic changes in the number and distribution of the eosinophile cells. The reaction exhibited by the blood is best described by the following experiments, of which the results have been repeatedly confirmed by observations to be cited later.

Experiment 1. A guinea-pig weighing 481 grams received pork containing 2000 trichinæ. The proportion of eosinophile cells in the blood and the weight underwent the changes indicated below:

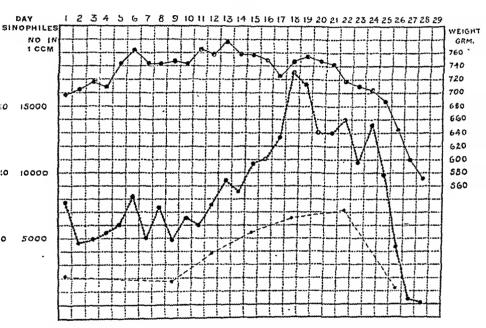
Day.		Eosino leuko	-	Weight.			Day.		Eosino leuko	Weight.		
lst.		1.3 per et.		481 grm.		1	34th.		5.0 p	er ct.		
9th.		2.5	"	496	**	;	43d .		4.0	64		
18th.		7.5	"			1	49th.		8.5	44	462 (	grm.
21st .		15.5	**	477	**		51st.		3.0			
25th.		6	44			ì	57th.		1.8	tt	439	"
32d .		10.5	"	509	et	j	65th.		1.3	• •	430	**

The animal finally recovered and regained its former weight. Experiment 2. A guinea-pig weighing 695 grams received 3000 trichine. The changes in the proportion of the eosinophile cells and their number in 1 c.mm. of blood are well shown by Chart I.

The record of the total number of leukocytes in 1 c.mm. of blood was as follows: First day, 13,900; ninth, 17,200; twelfth, 24,600; fifteenth, 25,300; eighteenth, 18,700; twenty-second, 25,900; twenty-sixth, 15,100. The proportion of eosinophile cells being known, their absolute number is readily estimated, and has been indicated in the chart.

During the first ten or twelve days after ingestion of trichinous meat there is no noteworthy alteration in the number of eosinophile cells; a gradual increase follows and reaches a maximum during the latter part of the third or the beginning of the fourth week. The number of eosinophile leukocytes may remain elevated several weeks, but should death ensue a more or less rapid decrease precedes the fatal termination. In one animal the blood contained 1.3 per cent. of eosinophile leukocytes at the onset of the experiment; in a second, 15.3 per cent., yet in the two experiments the number of eosinophile cells underwent similar changes.

#### CHART I.



Showing changes in the number of cosinophile leukocytes and of polynuclear leukocytes with fine granulation after infection with 10,000 triching. The percentage of cosinophile leukocytes is indicated by a dotted line; their number in 1 e.c. of blood by a broken line; the number of polynuclear leukocytes with fine granulation in 1 c.c. of blood by a broken and dotted line; the weight of the animal by a continuous black line.

According to the observations recorded by Leuckart¹ the encapsulated parasite in the muscle of the hog or other animal is set free by the action of the gastrie juice within three or four hours after it is taken into the stomach and, passing to the small intestine, attains sexual maturity within from thirty to forty hours. Before the end of the second day copulation has taken place, and on the sixth or seventh day ripe embryos are first observed in the interus of the female worm. At this time all of the female parasites have not

<sup>&</sup>lt;sup>1</sup> Die menschlichen Parasiten, Leipzig und Heldelberg, 1876, vol. il.

its maximum distention. On the ninth or tenth day after infection embryos have begun to reach the muscles. The foregoing experiments show that the eosinophile cells of the blood increase and reach a maximum at a time when embryonic trichinæ are passing in great numbers from the intestine to the muscles. The adult parasites in the intestine gradually diminish in number and have disappeared at the end of five or six weeks. In the guinea-pig the disease is apparently of shorter duration, for I have never found adult trichinæ in the small intestine after the fourth week of infection.

In Experiment 2, in which the total number of leukocytes have been repeatedly determined, leukocytosis has been found associated with increase in the proportion of eosinophile cells. When from the total number of leukocytes and the percentage of eosinophile leukocytes the number of the latter in 1 c.mm. of blood is estimated, the absolute and relative numbers are found to undergo corresponding changes: until the middle of the second week there is no increase, but subsequently the chart shows a gradual rise, which reaches a maximum on the twenty-second day. The maximum percentage of eosinophile leukocytes noted on the eighteenth day is apparently due to a diminution of the other leukocytes rather than to an actual increase of the eosinophile cells.

In the experiments to follow, guinca-pigs were infected with trichinæ in large number. Though death followed more rapidly than in the preceding experiments, the eosinophile cells exhibited changes similar to those already noted.

Experiment 3. A guinea-pig weighing 667 grams ingested pork containing 7500 trichinæ. Following is a record of the changes in weight and proportion of eosinophile leukocytes:

Day.			ophile eytes.	Weig	tht.	Day.					Eosine leuko	Weight.		
lst .		2.3 p	er ct.	667 (	rm.		11th				4.5 p	er ct.		
2d .		6.5	11	•		j	12th				2.0	66	610	grın.
3d .		8.8	"			,	13th				2.5	**	601	**
4th.		30	16			1	14tb				••••			
5th .		1.7	**	646	4.6		15th				9.2	"	606	66
6th .		0.5	* *				16th							
7th .		0.8	**	601	4.6		17th	,			12.0	"		
8th .		1.3	**	582	4.6		18th				••••			
9th .		03	**	576	**		19th				7.7	"	473	t t
10th .		0.5	**	585	4.6									

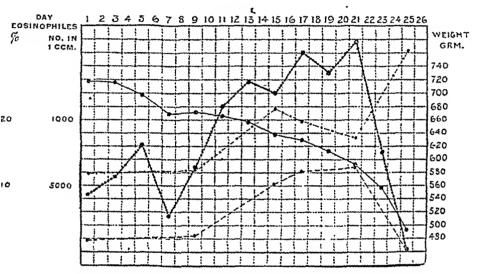
The animal died on the twentieth day after infection, and adult male and female trichinæ were present in immense number in the small intestine. Loosely coiled embryos were very numerous in the voluntary muscles.

Experiment 4. An animal weighing 718 grams received 10,000 trichine. The weight and percentage of eosinophile leukocytes are recorded in the accompanying chart. At the onset of the experiment the number of leukocytes per cubic millimetre was 10,800; on the ninth day the leukocytes numbered 10,200, but sub-

sequently increased and were as follows: Fifteenth day, 21,300; seventeenth, 20,400; twenty-first, 20,800. Shortly before death, which occurred on the twenty-fifth day, the number of leukocytes was 17,400. From the figures just given, together with percentages determined by differential count, the number of cosinophile leukocytes and of polymorphous leukocytes with fine granulation has been estimated.

By frequently repeated examination of the blood of his first patient infected with trichine, Brown demonstrated a remarkable relationship between the neutrophile and eosinophile leukoeytes.





Showing changes in the number of cosinophile leukocytes and of polynnelear leukocytes with fine granulation after infection with 10,000 trichinæ. The percentage of cosinophile leukocytes is indicated by a dotted line; their number in 1 e.e. of blood by a broken line; the number of polynuclear leukocytes with fine granulation in 1 e.e. of blood by a broken and dotted line; the weight of the animal by a continuous black line.

Daily estimation of the number of these cells in one cubic millimetre of blood showed that when the eosinophile eells increased the neutrophile leukoeytes exhibited a corresponding diminution in number, so that when the eosinophiles had reached a maximum percentage of 68.2 the number of neutrophiles in one cubic millimetre of blood was less than normal, even though there was at the time a marked leukocytosis.

In Experiment 4 the total number of lenkoeytes was markedly increased after the second week of infection with triching.

In Chart II. both cosinophiles and finely granular polynuclear leukoeytes undergo a parallel rise, but with further increase of the absolute number of cosinophile cells the finely granular leukoeytes exhibit the inverse relation noted by Brown. With the terminal decrease of cosinophile cells there is a very great increase of finely granular forms. It will be subsequently shown that increase of the eosinophile leukocytes in the blood is often associated with such great multiplication of eosinophile cells in the bone-marrow that other cells are in part replaced. It is not improbable that this great accumulation of eosinophile cells retards the multiplication of polymorphous cells with fine granulation, so that their number in the blood diminishes. It is, then, unnecessary to assume that diminution of finely granular leukocytes, accompanying increase of eosinophile leukocytes, is due to transformation of the former into the latter.

Decrease of Eosinophile Leukocytes with Severe Trichinosis. Charts I. and II. exhibit certain peculiarities which other experiments have shown are not accidental. With the less severe infection caused by 3000 trichinæ (Chart I.), the weight of the animal was maintained, indeed with a slight increase, during almost three weeks. The more severe effect of 10,000 trichinæ is shown by Chart II., where the weight of the animal gradually diminished from the onset of the infection. In this case the animal; which at first was large and healthy, survived twenty-five days, and the cosinophile cells, which rose more quickly than in the former experiment, reached approximately the same number. In other experiments, where trichinæ were administered in very large number, little resistance to the infection was shown, the weight of the animal diminished with great rapidity, and death followed within two weeks. The following experiments illustrate the condition:

Experiment 5. To a guinea-pig weighing 604 grams was fed pork containing 6500 trichinæ. The changes in weight and percentage of the changes o

centage of eosinophile cells were as follows:

Day.								Eo	sino	Weight.	
1st										10.3 per ct.	604 grm.
5th										5.7 "	590 "
9th										6.3 "	499 ''
12th										0.3 "	448 "

The animal died on the twelfth day after infection. In the

small intestine adult triclinæ were present in great number.

Experiment 6. A guinea-pig weighing 609 grams received 10,000 trichine. The animal had been infected seven months before with 2000 trichine, but had completely recovered and had gained 100 grams in weight. Death occurred on the seventh day of the second infection.

Day.				Eos	ino	phile leukocytes.	Wei	ght.
1st						22.3 per ct.	609	grm.
5th						0	532	"
7th						0	483	46

The small intestine contained adult trichinæ in immense numher, while in the muscles were encapsulated trichinæ in abundance. Experiment 7. A guinea-pig weighing 607 grams received 20,000 triebing:

Day.								Eo	sino	Weight.	
1st										7.7 per ct.	607 grm.
4th			•		•		•			03 "	517 "

Death occurred on the fourth day after infection, and adult trichinæ in great number were present in the small intestine.

In the experiments which precede those just described eosinophile eells of the blood have diminished with greater or less rapidity just before death. The weight of the animal doubtless gives the best indication of the effect of the infection upon its nutrition, and changes in weight can serve as an index of the power of resistance. The diminution in weight which precedes death is accompanied by a corresponding diminution in the number of cosinophile cells. This is well seen in Chart I., where the weight, after increasing during the first two weeks, subsequently falls, gradually at first, but later more rapidly. In Chart II., even though the weight gradually diminishes from the onset of infection, decrease of eosinophiles corresponds with a more sudden fall in weight. In Experiments 5, 6, and 7 the rapidity with which the resistance of the organism has been overcome is shown by the sudden fall in weight; the eosinophile cells rapidly diminish in number, and subsequent anatomical studies will demonstrate how injurious is the effect of the infectious agent upon these cells.

Local Accumulation of Eosinophile Cells. Several experimental studies have sought to determine the pathological changes produced in lower animals by trichina spiralis, and especial attention has been given to the muscle fibres invaded by the parasite. The purpose of the present investigation has been to study the relation of the leukoeytes and notably of the eosinophile cells to the parasite or to poisons produced by it. Since the eosinophile cells are increased in the blood the attempt has been made to determine how they multiply, where they accumulate, and what alterations they undergo. The final object of such study is to determine, so far as possible, what part the eosinophiles play in resisting invasion of an animal parasite.

According to Leuckart, whose view has long been accepted by pathologists, the embryos of trichina spiralis set free by the female worm within the lumen of the intestine make their way by aid of their own activity through the intestinal wall into the peritoneal eavity, and hence, following the loose connective tissue, reach the various voluntary muscles. Leuckart had rarely, if indeed ever, seen embryos free within the intestinal lumen. Cerfontaine and, later, Askanazy have shown that the mature female worm penetrates the mucosa and there expels her young. Transmission by

way of the lymphatic vessels through the mescnteric lymphatic glands and thoracic duct to the vascular system affords a simple explanation of the rapidity with which trichinæ are carried to the

muscles throughout the body.

The observations of Askanazy are of especial interest. Many female trichinæ pierce the villi, and in part, or with their entire body, enter the central chyle vessel, within which free embryos can be found; female worms also penetrate the mucosa, where they usually enter a lymphatic vessel. A few parasites apparently fail to find a lymphatic vessel and deposit their young within the mucosa, whence not improbably they migrate by their own activity through the intestinal wall into the peritoneal cavity. Repeated observations have, however, shown that the embryonic trichinæ, an insignificant number excepted, enter the lymphatic vessels and are carried to the mesenteric lymph glands, where, in rabbits, according to Askanazy, embryos are readily found during the latter part of the second week after infection. From the lymph glands by way of the lymph stream, trichinæ enter the thoracic duct and hence are carried through the heart and lungs to the systemic circulation, thus reaching, ten to fourteen days after infection, the voluntary muscles, which alone afford a suitable site for further development. In the lungs of infected rabbits Askanazy has rarely failed to find small red areas where the bloodvessels are dilated and hemorrhage has occurred into the alveoli; at a later stage fibrin and some leukocytes are present. Within such areas he has repeatcdly found embryonic trichinæ, which acting, he believes, as emboli, cause the lesion and afford further evidence in favor of a hæmal distribution of the parasite.

I have studied the relation of the eosinophile cells to the lesions of experimental trichinosis in a considerable number of animals, some dead as the result of infection, others killed at varying intervals after infection. In the four experiments to follow, a uniform dose of 2500 trichinæ was administered; the blood was examined at intervals of four days, and the animals were allowed to live periods varying from approximately one to four weeks. Subsequent observations made for the most part upon animals spontaneously dead after infection have shown that these experiments

fairly represent the course of infection.

Experiment 8. The animal was killed on the ninth day after receiving 2500 trichinæ.

Day,								Eo:	Eosinophile leukocytes.				ight.
lst										5.7 pc	er et.	487	grm.
5th	•									11.7	44	482	**
9th	•									11.7	**	484	**

Experiment 9. The animal was killed on the fifteenth day after infection with 2500 triching.

Day.	Eosinophile leukocytes.	Weight.	Day.	Eosinophile leukocytes.	Weight.
1st .	. 1.7 per ct.	336 grm.	13th .	. 10.7 per ct.	432 grm.
5th .	. 4.3 "	396 "	15th .	. 9,3 "	432 "
9th .	. 5.7 "	397 "		_	

Experiment 10. The animal was killed on the twenty-second day after infection with 2500 trichinæ.

Day.	Eosinophile Weight.	Day. Eosinophile Weight.	
1st .	. 5.7 per ct, 567 grm.	17th 15.3 per ct. 572 grm	1_
5th .	. 6.3 " 584 "	21st 19.7 " 570 "	•
9th .	. 2.0 " 566 "	22d 17.3 " 566 "	
13th .	. 6.7 " 579 "	}	

Experiment 11. An animal which had received 2500 trichinæ was killed on the twenty-ninth day after infection.

Day.	•	Eosinophil leukoeyte	13 C32/37L.	Day.	Eosinophile leukocytes.	Weight.
ist .		6.7 per ct.	. 586 grm.	17th .	15.7 per ct.	680 grm.
5th .		6.7 "	635 "	21st .	18.3 "	690 "
9th .		4.3 "	630 "	25th .	21.7 "	692 "
13th .		9.7 "	663 "	29th .	17.7 "	674 "

In accord with the observations of Cerfontaine and Askanazy upon the hæmal dissemination of the parasite, increase of the eosinophile leukocytes, previously described, is associated with local accumulation in the mesenteric lymph glands and in the lung. No noteworthy increase of these cells in the intestinal mucosa was noted, though in no instance was I so fortunate as to obtain a section through a worm which had penetrated into the mucous membrane. During the third week (Experiments 3 and 9), at a stage when triching are entering in large number the lymphatic vessels of the intestine, eosinophile eells accumulate in the lymphatic glands at the base of the mesentery, and may be collected in such numbers that they give the appearance of a small abscess in which ordinary polynuclear cells are replaced by cosinophile leukocytes. There is, however, no evidence of necrosis or of liquefaction of tissuc in such a focus. The occasional presence of numerous epithelioid cells, commingled with eosinophiles in the centre of the lesion, gives evidence that proliferation of the fixed cells may occur. At a later stage eosinophile cells disappear from the gland, in part at least, and in one instance (Experiment 12), in an animal which died during the sixth week after infection, cosinophile cells had almost completely disappeared, but small nodules of newly formed tissue, containing many epithelioid cells, apparently represented the lesion which at an earlier stage had been found infiltrated with

In one instance (Experiment 3) there was inconclusive evidence that accumulation of eosinophile cells was caused by the presence of an embryo of trichine. In the centre of a focus, where proliferating cells of epithelioid type were commingled with cosinophile

leukocytes, was a small amount of hyaline material. Indefinitely defined structure suggested the presence of a much altered parasite. In one instance an embryo was found within the mesenteric gland.

but eosinophiles were not numerous about it

Only in the lung does one find accumulations of eosinophile cells approaching in extent those of the mesenteric lymphatic glands. Embryonic trichinæ, or toxic products associated with their presence, after leaving the lymphatic glands would first reach this organ. Askanazy has directed attention to small hemorrhagic foci in the lung of rabbits infected with trichinæ and has been able to demonstrate the parasite within the lesion. Similar ecchymoses occur in the lungs of infected guinea-pigs after the beginning of the fourth At times the interalveolar capillaries are much dilated and red blood corpuscles have escaped into the alveoli. In one instance (Experiment 4) fibrin was also present and leukocytes, with eosinophile granulations, had accumulated in the periphery of the focus. In Experiments 10 and 11 the lungs contained small nodules of consolidated tissue in which eosinophile cells were massed in immense numbers. The alveolar walls were thickened and the alveoli were either filled by large desquamated epithelial cells or replaced by fibrous tissue. In the centre of the nodule eosinophile cells were so closely packed together that in sections stained with eosin the tissue had an almost homogeneously red color. In the walls of the adjacent alveoli eosinophile cells were scattered in countless number. In none of these lesions have I found trichinæ.

During the third week after infection triching are readily found in the voluntary muscles. The changes that follow their penetration into the muscle fibres have been carefully described in recent years by Ehrhardt and others. Degeneration of the fibre is associated with proliferation of its nuclei. At no stage of the disease have I found eosinophile cells even in small number in the neighborhood of the degenerate fibres. In this respect trichinosis

of guinea-pigs differs from that of the human subject.

MULTIPLICATION OF EOSINOPHILE CELLS. Examination of the blood has shown that the eosinophile lenkocytes, which begin to increase during the second week of trichinosis, reach a maximum during the latter part of the third week. These cells, which do not differ from those ordinarily present in the blood, are a little larger than the finely granular leukocytes and possess polymorphous nuclei. The eosinophile cells which accumulate in the lymphatic glands of the mesentery and in the lungs are identical in structure. Their nuclei are polymorphous and never give evidence of mitotic division. In the bone-marrow, however, eosinophile cells can be shown to proliferate actively.

During the first two weeks after infection the number of eosinophile cells in the bone-marrow is not notably altered, but at a later period the cellular elements are increased at the expense of the fat and the number both of eosinophile myelocytes and of forms with polymorphous nuclei is very greatly increased, while mitotic division is encountered much more frequently than in the normal marrow.

In a preceding article I have shown that the proportion of eosinoplule leukocytes in the blood of apparently healthy guinea-pigs is subject to great variation, the percentage count ranging from less than one to more than thirty. Corresponding to this varying proportion of eosinophile cells the bone-marrow exhibits noteworthy peculiarities. In animals of which the blood contains approximately 1 per cent. of eosinophiles fat is abundant and the cells of the marrow occupy the space between the fat cells. Cells with eosinophile granulation are fairly numerous and are in part myelocytes with eosinophile granulation, large cells with large, round, oval, or slightly irregular nuclei; in part smaller cells with polymorphous nuclei, resembling the eosinophile leukocytes of the circulating blood. In animals containing a higher proportion of eosinophile leukocytes, for example, 5 or 10 per cent., fat is somewhat less abundant and eosinophile cells form a much greater proportion of the marrow cells. Where, however, eosinophile leukocytes form from 15 to 30 per cent. of the white blood corpuscles the bone-marrow presents a characteristic appearance. Fat is largely replaced by myeloid cells, of which those with eosinophile granulation form a large proportion. Particularly numerous are myelocytes with eosinophile granulation. Similar cells in process of mitotic division, though never very abundant, are more numerous than is usual.

A brief description of the bone-marrow from Experiments 8 to 11, in which animals were killed at the end of one, two, three, and four weeks after infection with trichinæ, will show that the eosinophilia of trichinosis is accompanied by changes in the marrow similar to those just described. In none of these experiments did the proportion of eosinophile leukocytes equal 10 per cent. at the time when infection occurred. At the end of the first and of the second week after infection eosinophile cells are present in moderate number and mitotic figures are found only after continued search the end of the third week (Experiment 10), when, as has been shown, the eosinophile leukocytes of the blood attain a maximum, the fat of the marrow is largely replaced and eosinophile cells are present in very great number. Eosinophile myelocytes are particularly numerous, and dividing forms are abundant. figures are readily recognized by the hyperchromatic condition of the nuclei. The diaster stage of division is not infrequently encountered, while at times complete division of the cell body has occurred. At the end of the fourth week (Experiment 11) the appearance of the marrow is similar to that just described, but mitotic division is

somewhat less frequent in the sections. When an animal dies during the fourth week of infection the bone-marrow resembles that of animals killed at the height of eosinophile leukocytosis, even though the number of eosinophile leukocytes has diminished shortly before death. This fact is well illustrated by the bonemarrow from Experiments 2 and 4, where death has occurred on the twenty-eighth and twenty-fifth day after infection. Fat is largely replaced and eosinophile cells are present in very great number; eosinophile cells with polymorphous nucleus are, however, much more numerous than myelocytes, and only in the marrow from Experiment 4 has one mitotic figure been found.

The changes observed in the bone-marrow of guinea-pigs in which the eosinophile cells of the blood have been increased by trichinosis are comparable to those which have been found associated with the ordinary form of leukocytosis, in which the polymorphonuclear leukocytes with fine granulation (neutrophile in man, amphophile in rabbit) are increased. Ribbert first showed that the injection of micro-organisms causes an increase of the finely granular myelocytes and a diminution of fat in the bone-Roger and Josuć<sup>2</sup> studied the changes in the marrow accompanying suppuration and noted that an increase of the finely granular myelocytes, together with a diminution of fat, is caused by the injection of various toxic and infectious agents. Muir<sup>3</sup> has studied the changes in the bone-marrow consequent upon the repeated injection of staphylococcus pyogenes aureus into rabbits. Cellular elements increase at the expense of fat, and finely granular myelocytes, which divide by mitosis, are present in greatly increased number. Both Muir and Roger and Josué distinguished two types of cellular proliferation in the bone-marrow. When, as the result of hemorrhage or of abnormal destruction of red blood corpuscles, the nucleated red corpuscles proliferate by mitosis, the marrow assumes an appearance which is distinguishable from that associated with prolonged leukocytosis; an erythroblastic type can be distinguished from a leukoblastic type of marrow.

The experimental study of trichinosis has shown that the eosinophile leukocytosis of this disease is associated with changes in the bone-marrow which are analogous to those accompanying the more common leukocytosis caused by bacterial infection and by other means. The eosinophile leukocytes of the blood are derived by mitotic division from cosinophile myelocytes, which are analogous to the finely granular myelocytes. With continued proliferation of these cells their number in the bone-marrow so increases that; replacing the fat, they give a characteristic appearance to the tissuc. A coarsely granular or eosinophile variety of the leukoblastic type

<sup>&</sup>lt;sup>1</sup> Virchow's Arch., 1897, cl., 391.

<sup>&</sup>lt;sup>2</sup> Compt.-rend. Soc. de biol., 1896, p. 1038; and 1897, p. 322.

<sup>&</sup>quot; Journal of Pathology and Bacteriology, 1901, vol. vii. p. 161.

of marrow is then distinguishable from the more common finely granular variety.

DEGENERATIVE CHANGES IN EOSINOPHILE CELLS WITH SEVERE TRICHINOSIS. Infection with triching in such number that the animal survives or dies only after several weeks causes active multiplication of the eosinophile cells. Infection with a very large number of trichinæ; fatal within one or two weeks, is followed by rapid diminution of the number of these cells in the blood, and study of the internal organs from guinea-pigs used for Experiments 5, 6, and 7 have shown that the eosinophile cells under such conditions undergo degenerative changes which further indicate that the toxic products of the parasite exert a specific action on them. The organs obtained from animals used in the two following experiments, in which trichinæ in great number were administered, have been studied in order to confirm these observations.

Experiment 13. A guinea-pig weighing 648 grams was fed with pork containing 5300 trieline and died on the eighth day after infection. Adult triching were found in immense number in the small intestine.

Experiment 14. A guinea-pig weighing 679 grams received 7500 trichine. Two months before, the animal had been infected with 2000 triching and had completely recovered, the weight increasing almost 150 grams. Following the second infection the weight rapidly decreased and death occurred on the ninth day.

Day.								osinophile leukoeytes.	Weight.
1st .								. 0.7 per et.	679 grm.
5th.						٠		. 0.7 "	623 "
Oth					_				593 (6

Of much interest are the changes in the bone-marrow caused by rapidly fatal trichinosis. Here the number of eosinophile eells undergoes no noteworthy alteration, and both myelocytes and forms with polymorphous nuclei are present in moderate number. The nuclei of the myelocytes exhibit greater irregularity of outline than is usual, so that they not infrequently assume an irregularly lobed form, the size of the cell distinguishing it as a myeloeyte. Mitotie figures are oceasionally seen. The nuclei of the smaller cosinophile cells frequently stain deeply, are very irregular in outline and often have a shrivelled appearance. Particularly noteworthy is the presence of eosinophile eells in which the nuclei have undergone fragmentation. The number of such cells is variable, and those affected appear to be both myclocytes and polymorphonuclear forms. Throughout such a cell are scattered spherical globules of ehromatin, varying in size and staining deeply and homogene-The body of the cell appears to be unchanged, and the eosinophile granules take their usual brilliant stain.

Eosinophile eells, with similarly shattered nuclei, have been found in other organs. In Experiments 5 and 13 many eosinophile cells in the mucosa of the small intestine had undergone nuclear fragmentation, and the same process was observed in the mesenteric lymph glands. In one instance (Experiment 5) eosinophile cells were numerous in the mesenteric lymph gland, and at one point had accumulated to form an abscess-like focus similar to those already described; here nuclear fragmentation was particularly frequent.

Conclusions.—The administration of trichina spiralis to the guinea-pig causes an increase of the eosinophile leukocytes in the blood, comparable to that which accompanies human infection. There is no constant alteration of the number of these cells until the end of the second week after infection, when their relative and absolute number rapidly increases and reaches a maximum at the end of the third week. At this time embryonic trichine are in process of transmission from the intestinal mucosa by way of the lymphatic vessels and the blood through the lungs to the muscular system.

Eosinophile cells accumulate in the mesenteric lymphatic glands and in the lungs and form foci which resemble small abscesses in which polynuclear leukocytes are replaced by eosinophile cells. These cells are provided with polymorphous nuclei and do not differ from the eosinophile leukocytes of the circulating blood. Accumulation of eosinophile cells in the mesenteric lymphatic glands and in the lungs is explained by the transmisson of the embryonic parasite through these organs.

Increase of eosinophile cells in the blood and in other organs is accompanied by characteristic changes in the bone-marrow. The fat is diminished in amount, and cellular elements replace it. Cells with eosinophile granulation are present in immense number, and particularly numerous are the eosinophile myelocytes, cells peculiar to the bone-marrow, while such cells, undergoing mitotic division, are more numerous than usual. The bone-marrow is the scat of

multiplication of the eosinophile leukocytes.

The number of eosinophile leukocytes in the blood always diminishes before death, so that the proportion usually becomes less than 1 per cent.

Infection with a very large number of trichinæ causes a rapid diminution of the number of eosinophile lcukocytes and is quickly fatal. The eosinophile cells of the bone-marrow exhibit degenerative changes, of which nuclear fragmentation is most characteristic. Similar changes may affect the eosinophile cells of the intestinal mucosa and of the mesenteric lymph glands. Mild infection stimulates the eosinophile cells to active multiplication, but severe infection causes their destruction.

### A BRAIN TUMOR INVOLVING THE SUPERIOR PARIE-TAL CONVOLUTION; TWO OPERATIONS FOR ITS REMOVAL; PARTIAL SUCCESS, WITH SOME RELIEF OF SYMPTOMS; DEATH TWO YEARS LATER; AUTOPSY.<sup>1</sup>

# By Theodore Diller, M.D., (of PITTSBURG)

NEURGLOGIST TO THE ALLEGHENY GENERAL HOSPITAL; PHYSICIAN TO THE INSANE DEPARTMENT OF ST. FRANCIS' HOSPITAL.

CLINICAL SUMMARY. Man of good habits, aged fifty-six years; neurasthenic symptoms for one year; then during four years frequent attacks of Jacksonian epilepsy, initial convulsive movements beginning in the left great toe; general symptoms of brain tumor appear only after these attacks had been present for two years; two operations; tumor only partly removed because of hemorrhage; partial relief; death five years after onset and two years after the operation. Autopsy: A large spindle-celled sarcoma in the right superior parietal convolutions and adjacent mesial convolutions.—J. H., a man, aged fifty-six years, a druggist, had always enjoyed good health until the spring of 1898. His family and personal history were negative; he denied specific disease. No history of traumatism.

In the spring of 1898 he felt tired and often complained of weariness. Slumber refreshed him much less than formerly, being often disturbed by dreams. He often sung in his sleep. The patient frequently remarked that he "could not keep up with the procession." These neurasthenic symptoms continued until February, 1899 (i. c., about one year), when, without the slightest warning,

he was seized with an attack as follows:

His left great toe felt as though in a "cramp." This sensation continued for five minutes, when he sat down. By this time the foot began to twitch. This also continued five minutes. Then convulsive movements began to ascend the body, involving, in the order named, the muscles of the left side of the trunk, the neek, causing here a sense of choking, and, finally, the muscles of the chest and neck, especially those of the right side, the head moving forward and backward, striking with force against the floor. These convulsive movements were maintained without intermission from 1.30 to 5 p.m., when they ceased for a time. Soon there was a resumption of the movements in the left trunk, which, with intermissions, were kept up until 2 A.M. the next day. He was conscious throughout the attack, at times engaging in conversation. The arm and face were at no time involved in convulsive movements. During the

<sup>1</sup> A paper rend before the Allegheny County (Pa.) Medical Society, November 17, 1903.

attack he experienced a peculiar sensation in the left leg "like

electricity going through it."

Following this seizure, moderate but distinct loss of power in the left arm and leg were noted by the patient. He stayed in bed more or less for a period of three weeks, when he felt as well as ever, except for a certain loss of control of the left arm and some "clumsiness" of the left leg. Four weeks after this attack he was in better health than at any subsequent period.

Five weeks after the attack just described a second occurred; and this was followed by a third, fourth, and fifth seizure, the intervals between them being from ten to fifteen days. These attacks lasted from ten to twenty minutes each, and always began by twitchings in the left great toe, which marched up the leg, thigh, and trunk, as in the first attack. In no seizure was the face or arm involved in convulsive movements; but the latter felt numb and weak during the attack.

Now several attacks occurred in which the entire left leg was at once involved in convulsive movements. In a few attacks the

muscles of the calf or thigh seemed to be first involved

Since the first dozen attacks they have occurred at irregular intervals of from ten days to six weeks up to the time of the operation. The great majority of all these seizures began by convulsive movements in the left great toe; although others occurred in which the muscles of the entire left leg were apparently simultaneously involved.

Usually (not always) the patient could predict an attack from a few minutes to twenty-four hours in advance by a peculiar sensation in the leg. After each attack the left arm and leg were weak for a time; but usually recovered within the ensuing five or six days. Convulsive movements ceased in all muscles simultaneously.

His consciousness was entirely preserved throughout all the seizures. The left arm and face were never involved in the convulsive movements. The eyes never turned to one or the other

side during a seizurc.

The patient had never had headache, vomiting, vertigo, loss of vision, diplopia, or disturbance of hearing.

The last attack before the operation occurred in the latter part of April, 1901, and about twenty-six months after the initial seizure.

He went to bed complaining of a great sense of weariness and fell into an unusually heavy sleep. The next day he complained of severe headache located in the occiput. The next night he was taken with a severe seizure of the usual type while on the street. For thirty-six hours following he was dull, stupid, restless, delirious. The second evening after this attack, when he was examined by Drs. Montgomery, Stieren, and myself, he was still somewhat dull and clouded mentally; but when aroused he recognized members of his family and conversed a little. Palsy of the right third nerve

was apparent, as evidenced by a dilated pupil, external squint, and ptosis in the right eye. Dr. Stieren discovered optic neuritis of the right eye and an appearance suggestive of this condition in the left eye.

Close questioning of members of the family developed the fact that the patient was believed to have undergone moderate but progressive mental deterioration since the first convulsion, as evidenced chiefly by a growing lack of interest in affairs, dulling of perception, a lessened sense of responsibility, and a considerable loss of self-reliance. It also developed that the patient had suffered a progressive loss of power in the left arm and leg, aside from the temporary losses following the seizures.

Examination, May 16, 1901. There is in the median line of the skull posteriorly, about four or five inches anterior to the inion, two inches posterior to the Rolando fissure, a bony protuberance, which

his wife believes has grown during the last few years.

The mental condition is one of mild, moderate dementia. Memory is fairly good. He is somewhat careless in his habits. His interest in affairs has diminished. He does not read, go to church, etc., as formerly.

Muscular Sense and Stereognostic Appreciation. He recognizes objects placed within either hand readily. Stereognostic appreciation by his feet seems equal. Fingers of left hand, placed in various positions, are not correctly reproduced in right hand.

Special Senses. Hearing and eyesight normal. Taste normal. Eyes. No apparent extraocular palsy. He moves his eyes in all directions readily. Pupils equal; they react moderately but promptly

to light and also to accommodation.

Sensation. Temperature sense, normal; tactile, normal; pain, normal.

Motion. Grasp of left arm distinctly less than that of the right, probably about one-third less. There is about the same degree of

loss of power in the left leg.

Reflexes. Knee-jerks: right is normal; left is greatly increased. Ankle clonus absent on both sides. Plantar reflexes on both sides are very active. Babinski sign absent on both sides. Cremaster reflex present on both sides. Abdominal reflex absent on both sides. Bieeps-jerk: absent on right side; present on left side. Triceps-jerk: left, absent; right, absent also. Scapular reflex not obtainable.

Percussion. No difference in percussion note over the skull. More pain is produced over the protuberance on the skull previously

mentioned than elsewhere.

Viscera. Heart, lungs, and liver normal. Pulse 100.

Diagnosis. A tumor of unknown character in the superior Rolandic region of the right side involving the leg centre.

Operation, May 20, 1901, by Dr. R. W. Stewart, at the Mercy

Hospital.

It was proposed to make an opening, the centre of which should be over the right superior parietal convolution, just behind the Rolandic fissure and as near to the median line as possible; but when the flap of scalp was turned back, the long protuberance already referred to became very striking; and here the bone was found to be very thin, soft, and evidently discased; so it was hastily concluded to make the opening at this point—i.e., about one inch directly posterior to the point at first intended. This bony protuberance proved to be soft, spongy, thin, eroded skull, very dark in color, which was readily removed. The healthy dura beneath was incised when a tumorous mass was readily made out. But with beginningattempts to remove it the patient fell into a condition of collapse, due largely or wholly probably to a continuous and persistent oozing hemorrhage from the seat of the operation. The wound was, therefore, packed, and the operation hastily concluded. The patient recovered fairly well and seemed to be in good condition on the next day. A microscopic section of a portion of the tumor removed proved to be a spindle-celled sarcoma (Dr. Singley).

A second operation was undertaken by Dr. Stewart six days later, Drs. McKennan, Werder, Buchanan, Mayer, and others being present. As soon as the packing was removed a steady and persistent hemorrhage at once began, which repeated packings failed to coutrol. An enlargement of the opening in the skull failed to reveal cerebral convolutions at any point. Dr. Stewart was, however, able to get his finger between the tumor and the brain structure and thought the growth extended in a forward direction. After the removal of a number of small pieces of the tumorous mass, the operation was again hastily terminated, since the patient was again going rapidly into a condition of collapse. He made an uneventful

recovery from the second operation.

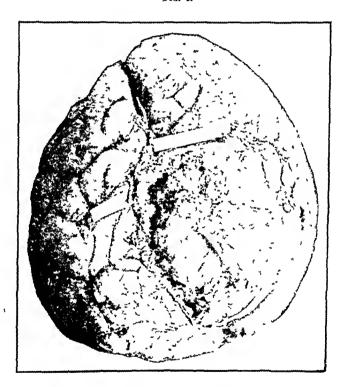
I examined the patient on July 25, 1901, when I found the wound well healed. He expressed himself as feeling brighter and happier than for several months past. He had resumed smoking, a habit he had given up some months before the operation because of a lack of desire for tobacco. Members of his family, too, regarded his mental condition as much improved. In the two months since the operation he had had two convulsive scizures of the usual type.

The patient lived a little longer than two years after this examination; but during this time he was not again examined by me. His family report, however, that for the most part he was fairly comfortable; that the convulsive seizures occurred with somewhat less frequency and severity than during the two years preceding the operation; that he was troubled with headache but seldom; and that he never vomited; that his eyesight seemed good; that he was hopeful, cheerful, and on the whole happy; that, although much improved mentally, a certain psychic reduction was noticeable; and that a certain degree of weakness of the left arm and leg was observ-

able (more at some times than at others). In short, both the patient and his family felt that he had been much benefited by the operation.

Last January he developed an attack of pneumonia, and following eonvalescence from this illness considerable increase of his mental reduction was noticed; and from this time on loss of power in his right arm and leg, especially the latter, steadily increased and became very marked. However, only a few days before his death he walked about the neighborhood with the aid of a cane and visited some friends. With the aid of his glasses he was still able to read a newspaper. Although he seldom complained of headache, he often spoke of a fulness about the head.

Fig. 1.



On July 31, 1903, he was seized with two general convulsions. Following the second attack coma developed, and death occurred on August 2d.

An autopsy was performed by Drs. Daggett, Litchfield, and myself sixteen hours after death. The sealp over the opening in the skull was found much depressed and united by thin cicatricial bands to the underlying structure, and these in turn to the tumor mass. Part of the tumor adhered to the skull-cap upon its removal.

The tumor was found to extend from the upper extremity of the Rolandic fissure to the parieto-occipital fissure, posteriorly. On

the convexity of the brain it extended downward to the upper portion of the inferior parietal convolution. On the mesial aspect of the brain it extended down to the upper third of the gyrus fornicatus. It bulged beyond the median line, producing a large concavity on the mesial aspect of the opposite lobe, at one point, over the paracentral convolution, giving off two tit-like projections, which produced deep indentures in the corresponding convolutions of the left side. The tumor, therefore, involved the superior parietal, the paracentral, and quadrate convolutions chiefly and the inferior parietal convolution and the gyrus fornicatus also partially. No other tumor was discovered.

The tumor was dense in structure and easily palpable in the fresh specimen from the surrounding cerebral tissue, and about the size

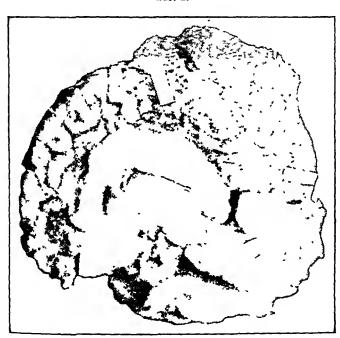


Fig. 2.

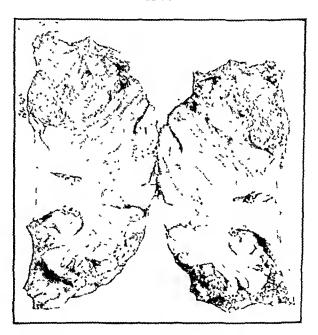
of a duck-egg. On section it offered great resistance to the knife. It was clearly defined from the brain tissue at all points. Immediately below the tumor, as shown by the section, the brain mass, for a depth of one inch, was somewhat softened.

REMARKS. In brief, we have here a sarcomatous tumor, the size of a duck-egg, situated in the right superior parietal, quadrate and paracentral convolutions, which had probably been growing for at least five years.

The first year of its growth the tumor had produced symptoms of a neurasthenic character only, during which time its diagnosis would

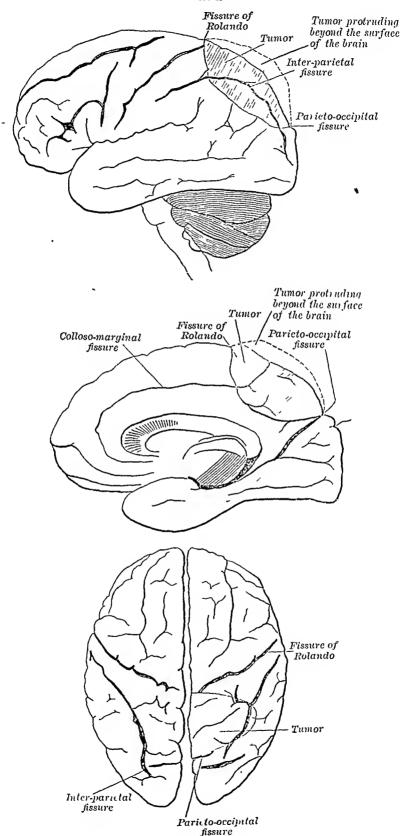
have been impossible. Fourteen months later Jacksonian epileptic attacks, with the signal symptom in the left great toe, began, and were maintained at intervals until death. Only three years later, or two years after the first of these attacks, did any other symptoms of the growth manifest themselves, the patient during this time being free from optic neuritis, headache, vomiting, vertigo, and eranial nerve palsies, the common symptoms of brain tumor; and so during this period a positive diagnosis of the growth was impossible. Nevertheless, even during this period the tumor had been strongly suspected. I saw the patient for the first time on November 14, 1899, with Dr. Litchfield, at that time the attending physician (i. c., about nine months after the initial seizure). Dr. Litchfield bad already reached the conclusion that the attacks of Jacksonian

Fig. 3.



epilepsy were due to an organic lesion, situated in the motor cortical region for the left great toe, and had urged an operation, with a view of exploring this region, having proven antisyphilitie treatment useless. I concurred in this view. Had Dr. Litchfield's advice been acted upon at this time or shortly afterward, it seems to me not unlikely, if not, indeed, probable, that the growth would have been successfully removed, since we must suppose it was then much smaller than it was at the time of the operation, eighteen months later, and since the point at which it was then proposed to trephine would have discovered the growth. Indeed, nearly all the favorable features for a successful operation were then present, viz.,

FIG. 4.



Diagrams intended to illustrate the position of the tumor,

a single hard, circumscribed sarcoma, moderate in size, non-infiltrating and situated in one of the most accessible areas for surgical intervention, and in an area which permitted the maximum of certainty in localization by the clinician.

These same favorable features were present at the time the operation was undertaken, eighteen months later, except that the timor was then doubtless larger. But, on the other hand, with the appearance of headache, optic neuritis, and stupor the probability that the organic lesion was a timor had grown to a practical certainty.

Even as it was, one cannot escape a feeling of disappointment that the growth was not entirely removed at the operations, since even then it was still an unusually favorable one for surgical intervention. But I will say no more of the surgical aspect of the case, since Dr. Stewart has kindly consented to offer some discussion of this phase of the subject; his remarks are appended to this paper.

Although the character of the tumor was not diagnosed, yet consideration of two features pointed to sarcoma, viz., the slow growth of the tumor and the fact that sarcoma occurs more frequently than any other brain tumor in adults. In a negative way the absence of carcinoma or tubercle in other parts of the body also lent support to this view.

As to the light this case sheds on ccrcbral localization, not a great deal can be said, because of the considerable size of the tumor, and since its exact starting-point cannot be known. In general, however, it conforms to the commonly accepted view that the cortical motor representation for the left great toe is situated in the opposite superior parietal convolution. It argues against the location of stereognostic appreciation taking place in this convolution. It also argues against the views of those who would place the motor cortical representation for the great toe in the superior precentral convolution—i. c., anterior to the Rolandic fissure; and, on the contrary, it affords support to the views of those who localize this function in the superior parietal convolution, well back of the Rolandic fissure. It will be remembered that the tumor extended anteriorly only to the Rolandic fissure.

If we may judge by the bony protuberance on the skull, the growth began midway between the Rolandic and parieto-occipital fissure, next to the longitudinal fissure.

A noteworthy feature of the case was the absence of some and the late appearance and temporary character of other of the general symptoms of brain tumor. Headache was severe once only, in the attack just before the operation. Vomiting and vertigo were never symptoms. The optic neuritis probably subsided, since no appreciable defect of vision was present at any time after it was discovered. The third nerve palsy was, I believe, correctly interpreted

at the time as a "distant symptom," and not due to direct involvement of this nerve or its nucleus.

One more point seems worthy of comment, viz., protrusion and erosion of the bone over the growth. The question arises in my mind, Was this due to the hard and unyielding character of the neoplasm which, by pressure, had shut off the blood supply to the superimposed cranial bone? It would seem so.

I am indebted to Dr. Litchfield for his notes on the earlier history of this case; to Dr. A. Létevé for the excellent photographs which illustrate this paper; and to Dr. R. W. Stewart for consenting to offer some discussion of the surgical aspects of the ease. To each of these gentlemen L desire to approach the plan.

of these gentlemen I desire to express my thanks.

### Remarks by R. W. Stewart, M.D.

The improvement, both in the mental and physical condition of this patient which followed partial removal of the tumor, makes it all the more regrettable that the whole growth was not enucleated. Had this been done, it is quite probable that there would have been a permanent recovery, as these growths are, as a rule, only semimalignant in character and with but little tendency to infiltration.

The difficulty which I experienced with this case was the alarming hemorrhage following the attempt at removal of the growth, which apparently had opened the longitudinal sinus. The hemorrhage was so severe that the patient immediately went into collapse, and a fatal issue was only prevented by packing the cerebral cavity and

the resort to hypodermic stimulation.

After the lapse of a week I was in hopes that the packing could be safely removed and the operation completed; but the attempt to do so was followed by exactly the same experience as in the former trial, and only a small portion of the tumor was removed at this time.

As the mieroscopic examination showed the tumor to be a sarcoma, and as no definite idea was obtained as to the limits of the

growth, no further attempt was made to remove it.

The light shed on the ease by the post-mortem evidence showed that the tumor was not inoperable, and I feel that I crred in two things. First, in not doing the operation in two steps as follows: First: removal of the skull over an area sufficiently extensive to expose the dura over the entire underlying tumor. The flap is then stitched back in position, and in the course of a week the second operation should be undertaken.

This eonsists in reopening the wound, incision of the dura over the entire extent of the tumor, and the eontrol of all hemorrhages as the operation progresses. In this ease it would probably have been necessary to ligate the longitudinal sinus at each side of the tumor. The tumor is then dissected out very much in the manner in which it is done in the post-mortem room, hemorrhage being controlled by ligation of the vessels as the operation progresses.

The chief advantage in doing the operation in two steps is that it minimizes the shock, which is the greatest danger confronting the patient. Had this been done and a sufficiently extensive area of the skull removed, it is probable that there would have been no opportunity for post-mortem findings in this case.

## CONGENITAL CYSTS OF THE FOURTH VENTRICLE.

A REPORT OF TWO CASES ASSOCIATED WITH TUMOR OF THE OPTIC THALAMUS AND CRUS CEREBRI.

## BY J. RAMSAY HUNT, M.D.,

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(From the Pathological Laboratory of the Cornell University Medical College.)

Introduction. The pathological conditions resulting in the formation of cysts within the fourth ventricle or a cystic dilatation of the ventricle are as follows:

- 1. Parasitic: Cysticercus or echinococcus cysts.
- 2. Cystic degeneration of a tumor.
- 3. Cystic degeneration of the choroid plexus.
- 4. Cystic dilatation of the fourth ventricle from occlusion of its communications.
  - Congenital cysts.

These are of pathological rather than clinical importance because of their rarity and the atypical character of the symptoms produced.

Both cases forming the subject of the present study are examples of brain tumor in young subjects with congenital cysts of the brain stem projecting into the fourth ventricle.

In both the intimate structural relation of cyst and tumor was demonstrable. 淵

#### SUMMARY.

Case I.—A boy, aged seven years, previously healthy, developed symptoms of brain tumor referable to the left optic thalamus. The important objective symptoms were: hemiparesis and hemiataxia of the right arm and leg; paralysis of the emotional innervation of the right side of the face; paresis of the left external rectus; nystagmus; hearing impaired on the right, both to aerial and bone conduction; no hemianopsia; no objective sensory disturbances.

Autopsy. Large tumor (mixed-cell sarcoma) situated in the left

<sup>&</sup>lt;sup>1</sup> Read in abstract at a meeting of the New York Neurological Society, January 5, 1904.

optic thalamus, infiltrating the subjacent structures and appearing

on the basilar surface of the pons.

The fourth ventricle is dilated by a large cyst, which is firmly attached to the floor, penetrates the substance of the pons Varolii, terminating in the midst of the neoplasm. Serial sections show the presence of glia and nerve fibres in all parts of the cyst wall continuous with the nerve structures of the pons.

History. A boy, aged seven and a half years, previous history negative, was admitted to the Montefiore Home September 12, 1896. Complains of headaches, vomiting, defective vision, uncertainty of gait, and an awkwardness of the right side; mentally clear, but apathetic and lacks energy; speech stammering; awkwardness and weakness of the whole right side; tongue deviates to the right. Station uncertain; gait ataxic; hemiplegic. Pupils medium size, the right larger than the left; all reactions prompt. Lateral nystagmus; slight convergent squint; vision  $\frac{3}{46}$  on both sides. Optic neuritis greater on the right side. Hearing both to bone and aerial conduction is impaired on the right. Percussion of skull negative. Smell and taste normal.

Note November 26, 1897. Is dull and forgetful; explosive laughter; hearing on right defective; skin reflexes active; tendon reflexes active and greater in the right side; right ankle clonus. The active innervation of the face is alike on the two sides. In repose and when responding to psychical and emotional stimuli, paralysis of the right side of the face is evident. Inco-ordination of the right arm and leg, which are flabby and thinner than in the left; no disturbance of sensation; left parietal region, slight tenderness on percussion. (Under antisyphilitic treatment the general symptoms subsided, including the optic neuritis, and the objective symptoms showed great improvement.) Discharged.

Readmitted April 9, 1900 (Dr. Abrahamson). Ataxia, atony, and weakness of the right side. The volume of the extremities is diminished on the right side. Asymmetry of the face; in repose the right side drooping; this inequality is reversed on emotional innervation, and disappears on voluntary innervation. Paresis of left external rectus with internal strabismus; lateral nystagmus; no hemianopsia; no limitation of visual fields. Vision: O. S.,  $\frac{20}{20}$ ; O. D.,  $\frac{20}{30}$ . No objective sensory disturbance; knee-jerks elicited by reinforcement, left > right; Achilles jerks lively; abdominal reflexes present, more active on the left side. Right ear defective to bone and aerial

conduction.

Note September 10, 1900. Apathetic and somnolent; vertigo, headache, and vomiting; pupils equal and rather small. The direct and consensual reactions to light on the left side are sluggish and

<sup>&</sup>lt;sup>1</sup> Patient was presented at the January meeting of the New York Neurological Society, and subsequently was reported clinically by Dr. Joseph Fraenkel in the Journal of Nervous and Mental Disease, 1899, p. 427.

at times absent; accommodation sluggish on both sides. Parcsis of left external rectus; nystagmus; knee jerks are variable, diminished, sometimes absent; Babinsky phenomenon on the right; Achilles jerks lively on both sides; no objective sensory disturbanees; abdominal reflex is absent on the right, feeble on the left.

Grew rapidly worse; progressive increase of the general cerebral

symptoms. Died September 30, 1900.

Autopsy. Only the brain was removed. The skull, meninges, and vessels of Willis were normal. The pons contains a tumor within its substance on the left side throwing its normal contour into irregular nodulations. The left fifth nerve at its exit from the pons is compressed and flattened, while the left third, fourth, and

sixth nerves stand in dangerous proximity to the growth.

Section through the hemispheres on a plane with the corpus callosum exposes a large tumor situated in the left optic thalamus and continuous with the infiltration in the pons. (Fig. 1.) It measures three inches in the longitudinal and two and one-half inches in the transverse diameter, and is rather sharply circumscribed from the surrounding brain substance by a lamellated periphery. It is of firm eonsistency and of a deep-red color (hemorrhagie). Some portions, chiefly on the periphery, are of a pinkish hue; others of a translucent appearance.

Hemorrhagic dots and minute areas of necrosis are scattered over the surface of section. The growth bulges into the third ventricle, the middle commissure of which is flattened out into a thin membrane, and encroaches posteriorly on the corpora quadrigemina.

The pineal gland is enclosed in a dense accumulation of connective tissue, but is otherwise normal. The hypophysis cerebri

was normal.

On separating the medulla and the cerebellum at the foramen of Magendi a firm epiglottis-like prolongation appears. This on removal of the right lobe of the cerebellum is found to be the posterior tip of a large cyst, filling up and distending the fourth ventricle. (Fig. 1.) This cyst is one and three-quarter inches long and one and one-half inches wide. Its walls are thick, wrinkled posteriorly, smooth, and distended anteriorly and laterally. The outer layer of the wall strips readily, as in a fibrinous exudation, exposing a smooth surface with prominent and injected vessels beneath. It is accurately moulded to the interior of the fourth ventricle and on its basilar surface is firmly attached to the floor. The attachments of its upper surface to the eerebellum are slight and casily separated. The width of the vermis of the eerebellum is reduced by pressure to five-eighths of an inch and the lateral recesses appear as deep excavations.

The medulla is broader and flatter than normal. The posterior orifice of the aqueduct of Sylvius is free. The whole ventricular system of the brain is distended, more so on the left side. Numerous

ependyma granulations. A small portion of the cyst wall was cut away, exposing the interior, which was smooth, containing only a

small quantity of clear fluid.

Microscopic Examination. The medulla, pons, left hemisphere of the cerebellum, and the enclosed cyst were hardened and embedded in bulk and cut serially. Approximately every tenth section was prepared and mounted by the Weigert-Pal method; half of these were subjected to a contrast stain (acid-rubrin).

Cyst. The cyst begins on a level with the tip of the calamus scriptorius, gradually increasing in size to the plane of the striæ acustica. From this level it becomes smaller and the walls thicker, dipping down into and becoming an integral part of the left side of the pons. On a level with the posterior corpora quadrigemina it terminates as a small triangular cleft, in the neighborhood of the left pyramidal tract.

From the tip of the thalamus to the striæ acusticæ the cyst wall has no connections with the floor of the ventricle, save to the ala pontis (ponticulus) on either side. From the striæ acusticæ to its termination the cyst wall is intimately associated with the neural

structures of the pons.

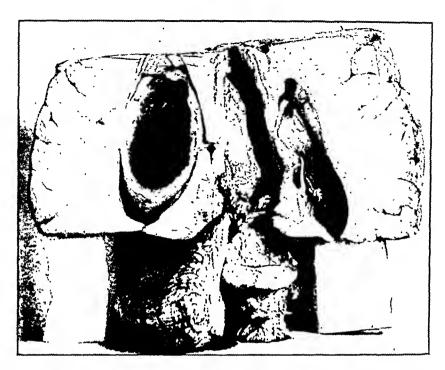
The nerve tracts form a decussation on its under surface, which pass upward into the cyst wall on either side. (Figs. 2, 3, and 4.) The cyst wall may be divided into three layers. An inner one is composed of glia; a thick middle layer of medullated nerve fibres which encircle the wall as a heavy band; and an outer layer in which the network of medullated nerve fibres is sparse, resembling gray matter. No ganglion cells could be demonstrated in the cyst wall, which possessed a rich supply of bloodvessels. No ependyma cells could be demonstrated lining the cyst wall. Here and there flat cells were seen, apparently of epithelial origin.

Cerebellum. The vermis and hemispheres of the cerebellum were compressed, and as a result showed changes in their configuration

but without atrophy.

Medulla and Pons. The left pyramidal tract is small and pale. The lemniscus and fasciculus long. posticus are normal on both sides. The columns of Goll and Burdach are paler than normal, probably due to ascending intramedullary posterior root degenerations. (As the cord was not removed this cannot be definitely

The medulla, except for a moderate flattening and lateral elongation, maintains its normal configuration to a level with the acoustic nuclei. Here the cyst becomes incorporated with the floor of the ventricle on the left side, nerve fibres decussating on its under surface and passing up into the cyst wall. This decussation is largely formed of the coarse fibres composing the middle peduncles of the pons, and increases considerably as the level of the superior olive is approached. Tegmental fibres, as well as a few fibres from



Case I.—Tumor of left optic thalamus and congenital cyst distending the fourth ventricle.





CASE I.—Weigert-Pal method. Level of strice neustices. Showing intimate relation of eyst wall to floor of ventriele.



CASE I.—Weigert-Pal method. Level of the superior olive. Showing thick band of medullated nerve fibres in wall of cyst, continuous with the neural structures of the pons.





Case I.—Weigert-Pal. Level of the posterior corpora quadrigemina. Cyst terminating in tumor as a narrow cleft.

the left median fillet and fasciculus long, posticus may be traced upward into the wall of the cyst.

At a level with the superior olivary body, where the cyst begins to sink gradually into the pons, the number of nerve fibres decussating on its under surface and passing up into its walls is very large. Most of these are derived from the pontine pedincle, so that these fibres on the right side of the pons are comparatively sparse.

Notwithstanding the distortions and changes in the configuration of this area, the important structures may all be discerned—i. c., the superior olive, the ascending root of the fifth, lemniscus, and the

faseiculus long. posticus.

On a level with the posterior corpora quadrigemina the cyst has tapered off to a small triangular slit in the region of the left pyramidal tract, and is here completely encircled by the tumor, which

projects ventrally as a nodular swelling. (Fig. 4.)

Tumor. The pontine tumor and the large thalamus tumor are continuous and have the same histological peculiarities—i. c., a polymorphous cell sarcoma, composed of round cells, spindle cells, and giant cells. The growth is extremely vascular, with numerous hemorphages.

Case II. Summary. A boy, aged seventeen years, previously healthy, following a head injury developed symptoms of brain tumor referable to the right crus cerebri. Weber's syndrome; left hemiplegia with extreme spasticity; complete right and partial left oculo-

motor paralysis; explosive laughter.

Autopsy. Glioma of the right crus cerebri extending posteriorly and infiltrating adjacent structures in the pons. A cyst of the fourth ventriele penetrating its floor, perforating the substance of the pons beneath and distinct from the aqueduct of Sylvius and appearing on the under surface of the right erms, terminating in the tumor mass.

Microseopically the eyst wall is composed of medullated nerve fibres and glia continuous with the nerve structures of the pons.

History. M. H., admitted to the Montefiore Home November 8, 1901; cash boy, aged seventeen years; family history negative. Previous history: was always a healthy boy, not subject to headaches or vertigo. (Would frequently become nauscated while riding in street cars.)

On June 7, 1901, he was hit in the back of the head by a swinging door, falling down a short flight of stairs. He received a scalp wound in the occipital region, but was not meonseious and in a short time was able to return home. In the street car, as had happened frequently before, he became nauscated and vomited. For a day or so he had moderate headache and in three days was able to return to his occupation apparently as well as ever.

One month later internal strabismus of right eye with ptosis

developed and was soon followed by a weakness- and-stiffness in the left arm. The weakness in the arm increased and became apparent in the left leg as well. He was inclined to somnolence and got very dizzy, but no headaches or vomiting. About the same time it was noticed that he laughed inordinately on slight provocation and sometimes spontaneously.

The patient was examined in the neurological department of the German Hospital and was referred to the surgical ward for operation, under the supposition that a post-traumatic cyst had developed at the base of the brain in the region of the right crus cerebri.

Operation August 28, 1901. An osteoplastic flap five inches in diameter was thrown back; the middle meningeal artery was resected and, after retraction of the temporal lobe, four exploratory punctures were made in the direction of the right crus, with negative results.

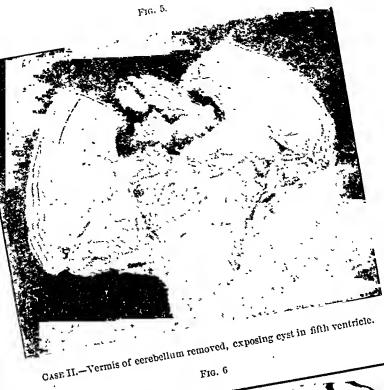
Discharged November 7, 1901, unimproved.

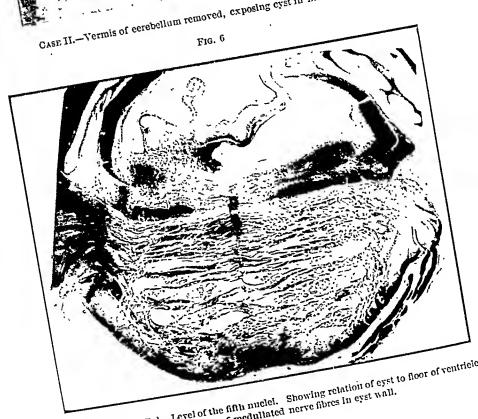
Status præsens, November 9, 1901. Head dolichocephalie; facc asymmetrical; teeth viciously implanted; torus palatinus; complete ptosis of right eye, partial of left; divergent strabismus on both sides; paralysis of the upward, downward, and inward movements of the right eyc. The inward and downward movements of the left eye are limited in their excursion and accompanied by nystag-Nystagmoid twitchings were present in the right eye on attempted movement. The right pupil is widely dilated and fixed. The left pupil is normal in size and all reactions are present but sluggish. Paralysis of the left face, arm, and leg, with spasticity; clonus; Babinsky phenomenou; no objective sensory disturbances. Skin reflexes were absent on the left side; hearing, smell, and taste normal; no limitation of visual fields. Station; body is bent toward the left side with a tendency to fall in the same direction. There was uncontrollable and involuntary laughter from time to time, especially when starting to speak. Mentally, he was bright and clear; speech normal.

Optic Nerves. The vessels of the disks were congested and the

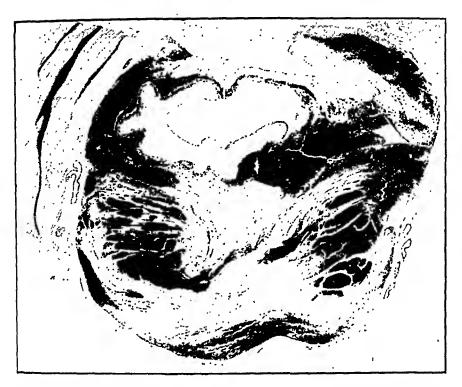
upper margin was hazy; urine negative.

Note, March 12, 1902 (Dr. Abrahamson). General condition is much worse. His speech is indistinct. Any question or command induced uncontrollable laughter; no weeping. The right arm and leg are the seat of slow co-ordinated movements, which may be controlled on command. The cessation is only temporary, There is contraction of the left upper extremity, the clenched hand resting in contact with the shoulder; extensor contraction of the left lower extremity. The tongue deviates toward the left. There is complete ptosis of the right eyelid and partial The right eye is turned upward and slightly outward, the only movement preserved being feeble external rotation. The left eye is turned outward and downward, with preservation of the exeursions downward and inward. Right pupil is large, with





CASE II.—Weigert. Pal. Level of the fifth nuclei. Showing relation of eyst to floor of ventricle and thick layer of medullated nerve fibres in eyst wall.



CASE II.—Level of the posterior corpora quadrigemina. The cyst is beneath and distinct from the aqueduct of Sylvius, the roof of which is torn across. Cyst wall has collapsed on one side. Gliomatous infiltration of pons.

F1G. 8.



Case II.—Welgert-Pal. Showing erus eerebri, optle tract and chasm; basal ganglia, internal capsule, and a portion of temporal lobe. Cleft in crural tumor representing termination of eyet.

irregular outline, and fixed. Left pupil is normal in size, with

sluggish reactions. Other cranial nerves are negative.

Note, July 12, 1902. Emaciation is most extreme. hand and arm are in extreme flexion contracture, the hand resting on the acromion; left leg shows extension contracture. The left side of the body is cooler than the right. He hears and attempts to respond to some questions, but the response is inarticulate and indistinguishable. During the past four months there have been no paroxysms of forced laughter. He can tell the number of fingers held before either eye. The patient leads a purely vegetative existence; never speaks; sleeps most of the time; points to the month to indicate desire for food or drink. He recognizes members of the family and calls them by name. He drinks large quantities of water, and for three months has passed urine and feces in the bed, and if not watched will carry excrement to his mouth. The movements of the tongue and palate are slow and feeble, but there are no evidences of cranial nerve palsies other than those mentioned, with the exception of the motor portion of the right trigeminus nerve, the jaw deviating toward the right side. Pain impressions are equally keen on both sides of the body; no albumin or sugar in the urine.

Autopsy Cadaver is in a state of extreme emaciation; sacral and trochanteric decubitus; tubercular focus in left apex; central pneumonic area in the left lower lobe. Chronic cystitis; otherwise the examination of the thoracic and abdominal contents was negative. There was incomplete union of the osteoplastic flap at the site of the operation. The dura mater over this region is thickened and adherent and the inferior surface of the right temporal lobe shows old superficial foci of softening, with pial thickening. The sinuses of the dura and the vessels of Willis are normal; moderate

internal hydrocephalus.

Description of Crural Tumor and Cyst. Springing from the right crus cerebri is a firm, nodular, grayish-white mass filling up the interval between the cerebral peduncles. The onter side of the growth is in close relation with the right optic tract; the inner side encroaches on the third nerve. The right third nerve is compressed and atrophic. The basilar surface of the pons and medulla oblongata with their respective cranial nerves are normal in appearance.

On splitting the cerebellum to afford inspection of the interior of the fourth ventricle, a cyst is disclosed springing from the anterior portion of its floor, to which it is firmly attached. (Fig. 5.) The posterior orifice of the aqueduct of Sylvius is free. The cyst is flattened and measures one and a quarter inches in its long and about five-eighths of an inch in its short diameter. The cyst wall is tough and dense and the surface is wrinkled. The interior is smooth and the only contents a clear fluid. The ependyma of the ventricle is dotted with numerous granulations. The cyst wall, at its attachment to the ventricular wall, dips down into the substance

of the pons, through which it passes beneath the aqueduct and appears on the inferior aspect of the right crus cerebri, where it stands in immediate relation to the tumor. The growth is firmly adherent to the superior wall of the cyst, which is collapsed in this region.

Microscopic Examination. A series of sections was prepared from various levels of the medulla, pons, and crus cerebri, including the cyst, according to the Weigert-Pal method with contrast stain. The medulla shows atrophy of the right pyramidal tract; the right spinal trigeminus root is normal. The central canal in the lower portion is obliterated and Helweg's tracts are degenerated. In the pons at the level of the fifth nucleus the eyst wall becomes firmly attached to it, forming an integral part of the floor of the ventricle. Numerous bundles of nerve fibres pass into and encircle the eyst wall, which contains a rich supply of medullated nerve fibres and glia cells. (Fig. 6.) The fasciculi long. postici are contained in the left wall of the cyst at its junction with the floor. The right fifth nerve root is atrophic. At this level no evidence of tumor infiltration is seen.

On a plane with the trochlearis nucleus the cyst is enclosed within the substance of the pons below the aqueduct, with which it has no communication, and a little to the right of the median line. (Fig. 7.) The configuration of the surrounding parts has been somewhat distorted; the important structures are, however, easily discernible—i. e., the median and lateral fillet, the roots of the cerebral trigeminus and the trochlearis, and the trochlearis conjunctivum. The latter is displaced toward the left side. The dense bundles of the faseiculi long. postiei are distributed over the superior portion of the cyst wall. At this level, below the lemnisci, infiltrating gliomatous tissue is already apparent.

Sections through the right crus cerebri include the thalamus, the lenticular nucleus, optic tract, and chiasm, and the inferior convolutions of the temporal lobe. (Fig. 8.) The normal outline of the crus is obliterated and is replaced by a tumor mass. On the under surface of and attached to the growth is the collapsed cyst wall. In the wall of the cyst medullated nerve fibres are still demonstrable. The wall is composed of a coarse, wavy glia tissue in which the fibrillar elements preponderate, and containing a sparse network of medullated nerve fibres. At several points lining the interior distinct areas of columnar epithelial cells are seen resembling

the ependymal lining of the ventrieles.

The tumor proliferation begins in the outer layers of the cyst wall and is here firm in texture, the spindle type predominating, forming interlacing waves and bands; numerous giant eells. In the periphery of the growth the proliferation is more typically gliomatous, merging gradually into normal areas. The vascular supply is rich.

The cyst wall may be roughly divided into two layers, the inner

composed of coarse glia and an external rich in medullary nerve fibres. The interior lacks a continuous epithelial lining, but a few remnants still persist. These consist of columnar cells, flat cells, and stratified layers of cells, the latter suggesting an epithelial

metaplasia. No ganglion cells were observed.

Remarks. The occurrence in the brain of congenital cysts, while rare, is recognized in all classifications of the subject. They originate in offshoots of the primary cerebral vesicles. Bruns mentions, in connection with gliomata of the pons, the occurrence in the brain stem of minute cysts lined by ependyma and evidently separations from the primary neural tube. Stroebe demonstrated in gliomata of the brain minute cysts lined by columnar epithelium, probably sprouts of the primary cerebral vesicles.

In spinal cord pathology the relation of central gliosis, gliomata, and syringomyelia to developmental defects and embryonal rests of the central canal is fairly well established. In brief, abnormal offshoots and diverticula of the primary neural tube in any portion of its course may furnish the incentive to morbid proliferation.

Cysts of the size, location, and nature just described are unique in my pathological experience. A parasitic origin could be definitely excluded by the nature of the histological findings.

In favor of a congenital origin are:

1. The eyst wall throughout was composed of medullated nerve

fibres and glia.

2. The intimate relations of the cyst wall with the adjacent nerve structures as it traverses the brain stem; the cyst is not intercalated, but forms an integral part of the pons.

3. Remnants of an epithelial lining.

4. The associated neoplasms.

5. The absence of cerebral symptoms preceding the development of tumor.

The gross anatomical relations of the cysts in my eases suggest an origin from that portion of the medullary tube engaged in the

formation of the second and third primary eerebral vesicles.

The developmental changes in these vesicles, which form the midbrain and hind-brain, are especially conspicuous and complicated. This portion of the fetal brain is wedged in between the head and neck bend, flaring out laterally to form the expansions of the floor of the fourth ventricle, corresponding to the lateral recesses.

The evaginations of the Rauten lippen, which develop subsequently, enfolding and covering in the ventral and dorsal zones of His, further complicate matters and would favor the occurrence of developmental defect. The frequency of gliomata in this region

is well known

In conclusion, I would emphasize the importance of subjecting the so-called old, sterile, parasitic cysts in the neighborhood of the ventricular cavity, to serial study and the Weigert method before excluding a congenital origin.

# A CASE OF ACCIDENTAL POISONING BY AN UNKNOWN QUANTITY OF ATROPINE SULPHATE; RECOVERY.

## BY SAMUEL STALBERG, M.D.,

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THE great majority of the cases of belladouna poisoning are aecidental in origin. Thus, of 466 recorded cases of poisoning by belladonna and its alkaloid, collected from medical literature by Witthaus, the drug in 344 cases was taken by accident, either in mistake for some other preparation or in overdose through some error of the druggist. In 35 cases it was administered with either homicidal or suicidal intent, while in 87 cases the cause was uncertain.

Following is a history of my case:

D. L., Hebrew, aged fifty years, has been suffering for several years with a chronic bronchial cough, accompanied by profuse expectoration. For this he was given, in a local dispensary, a pill, to be taken t. i. d., and containing, as I subsequently learned, strychnine, <sup>1</sup>/<sub>60</sub> grain; codeine, <sup>1</sup>/<sub>2</sub> grain, and atropine sulphate, <sup>1</sup>/<sub>240</sub> grain.

He had taken thirty of these pills during two weeks, when, being improved, he was advised to have his prescription renewed. This he did, taking the first pill of the second instalment on the evening of December 30, 1902, after having intermitted their use for two days. He took the second pill of this lot—the pill that no doubt contained the overdose—at about noon of the next day, and the toxic effects of the atropine began to manifest themselves about an hour later, when I was hastily summoned by the patient's daughter, who declared that her "father lost his voice."

Upon arrival I found the patient on his feet; at times attempting to stagger across the room; at others, stooping and supporting himself on the bed-post. His eyes were wild, brilliant, and staring, and the pupils dilated to their utmost. I do not remember, however, having noticed diplopia, amblyopia, or other disturbances of vision often seen after an overdose of atropine. Face was flushed, and somewhat expressive of terror. Fingers were restless, continually buttoning and unbuttoning the vest, suspenders, etc. He several times bent under the bed, as if in search of something. He was semidelirious, and chatted continually and incoherently. Several times he exclaimed: "Let me bark! I want to bark!" His voice was husky, and his mouth, tongue, and pharynx parched. He had a constant desire to micturate, and passed a quantity of urine every few seconds.

Temperature was normal; pulse 120; respiratory rate not observed. Patellar reflexes exaggerated.

At first puzzled as to the eause of the man's behavior, the thought of some drug intoxication soon suggested itself, and, upon inquiry, I found that he had been taking the above-mentioned pills. I immediately thought of atropine, and, telephoning to the drug-store, learned of their contents.

The diagnosis established, the indications for treatment were clear. Obviously, it was too late for the exhibition of chemical antidotes, and stomach-washing was impracticable. Pilocarpine hydrochlorate and morphine sulphate, somewhat antagonistic physiologically to atropine, were therefore immediately administered. Onesixth of a grain of the former and one-eighth of a grain of the latter were given in solution, per orem.

The morphine was repeated in about twenty minutes, and the piloearpine hourly for three or four hours. The drugs were exhibited in this manner rather than by the more prompt hypodermic method, for the simple reason that the soluble hypodermic tablets were unobtainable—an argument for the necessity of every physician to be equipped and ready for any emergency. The difference in the rapidity of action, however, could not have been great, since both pilocarpine and morphine, especially the latter, are rapidly absorbed from the stomach.

According to Kerr,<sup>2</sup> the physiological effects of morphine may manifest themselves in from two to three minutes when the drug has been taken hypodermically, and in four to five minutes after it has been swallowed in solution. I also eatheterized the patient, with a view to prevent reabsorption of the poison from the nrine, but without suecess. Of course, he was ordered to bed, but there was trouble in keeping him there.

Probably as a result of the morphine he slept a while, but his sleep was interrupted and restless. By 6 P.M. of the same day most of the alarming symptoms had either entirely disappeared or were greatly improved. He was no longer delirious, and spoke rationally, but his voice was still rough, mouth dry, and pupils dilated. The latter did not come down to normal for about seven days, and his pulse rate kept above normal for the same period. During, and for a few days succeeding the attack, the heart action was weak, so that, partly at the suggestion of Dr. A. A. Eshner, who was ealled in consultation, varying quantities of stryehnine and digitalis were administered after the subsidence of the acute attack. The test for sugar in the urine of the patient, taken during the attack, was negative; but this may have been due to the fact that the urine had been standing for a few mouths —owing to the illness of the writer—before the test was made. Raphäel's reports the exerction of 0.4 per cent. sugar in the urine of a man moderately poisoned by atropine.

This ease, as is seen, is a fairly typical one; but there are a few

features which deserve comment. In my case the temperature was normal. This is contrary to what usually obtains. In 19 reported cases in which the temperature was recorded, there was in every instance an increase in temperature of from 1° to 6° F. Others, like Boehm, Schaunstien, Kobert, and Schroff, hold that there is always a constant diminution in the body temperature in atropine poisoning. In a case of atropine poisoning recently reported by Cortright, the temperature was supernormal for about sixteen hours from the time of poisoning, the highest temperature being 103.03° F. Looking at this question from the point of view of the physiological action of atropine, we find that moderate doses cause a pronounced rise in temperature, while large toxic doses lessen animal heat.

According to H. C. Wood, this increase is due to paralysis of thermogenetic inhibition. According to Ott and Collmar, this increase is due to increased heat production, the result of stimulation of the thermogenetic centres in the spinal cord. The final fall in temperature is probably due, according to H. C. Wood, to vasomotor paralysis. The rise in temperature in atropine poisoning would seem to be a perfectly logical outcome, however, of the chief, characteristic, ultimate effect of the drug, viz., that of a paralyzant of inhibition. Another unusual feature of this case is the frequent and free micturition during the attack. Usually, as a result of the depressant action of the drug on non-striated muscle fibres, there is retention. A few cases, however, have been reported in which this frequent urination was present

frequent urination was present.

The present status of opinion regarding the place of morphine in the treatment of atropine poisoning is important. Among others, Reichert, as a result of experimental work, holds that morphine and atropine, far from being antagonists, are synergists, atropine there-

fore being of very limited utility in morphine poisoning.

In regard to atropine poisoning itself, he<sup>11</sup> believes that death in that case results from paralysis of the respiratory centre, but that the centre has great recuperative power, so that if artificial respiration is properly practised the centre recovers its activity, when there is in consequence a marked improvement of other depressed states.

Pilocarpine is considered a most efficient antagonist to the poisonous action of belladonna, the action of the two drugs upon the heart having been demonstrated<sup>12</sup> to be directly opposite, pilocarpine restoring the inhibitory action of the vagus after it has been destroyed by atropine. Pilocarpine also promotes the action of the sudoriparous and salivary glands, and is supposed to favor the excretion of the poison by its action on the emunctories. Symptomatic treatment is also of great importance in atropine poisoning.

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# THREE CASES OF PERNICIOUS ANÆMIA, WITH A DESCRIPTION OF THE PATHOLOGICAL CHANGES FOUND IN THE SPINAL CORD.

# BY ROBERT REULING, M.D.,

CASE I.-W. H., male, aged forty-six years; white, born in the United States; widower. Was seen by me in consultation during December, 1901. His occupation has been variable. For several years he was clerk in the Baltimore & Ohio Railroad office. For six years he travelled as salesman for a commercial house, and at thirty-five years he settled in South Carolina, where he started a small general store in one of the small towns in the northeastern part of the State. His family history is negative. No history of tuberculosis, anæmia, or neuroses. He has always lived fairly well, but in his occupation as salesman his food was frequently not of the best, and he had frequent attacks of gastric discomforts. His stomach became so deranged that his general health was much affected, so that he gave up his position as salesman and went into business for himself. As a child when six years old he had scarlet fever. Pnenmonia when seventeen years old. No sequelæ. From his nineteenth to his twenty-third year he was very nervous, apparently suffering from sexual neurasthenia. Gonorrhœa at twenty-two years, without complications. No history of syphilis or its secondary manifestations.

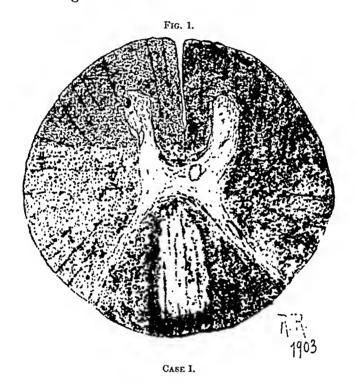
The patient dates his present illness from an attack of fever and marked malaise, associated with severe muscular pains, which was pronounced influenza by the attending physician. This was in November, 1899. He remembers several people that were similarly affected in the town; he was living in South Carolina at the time. He remained in bed for almost three weeks, and from his description the myalgia must have been unusually severe; the pains were espe-

cially marked along the spine and in the muscles of the legs. The fever was high and lasted about six days. There was gastric disturbance, marked nauséa, but no vomiting. Bowels constipated. On leaving his bed he felt extremely weak, very depressed, and had lost much flesh. After two months he began to feel somewhat better. but he was still not the same man, and anorexia, with mental depression, was still present. About six months after this illness he was taken suddenly ill with severe pains in the abdomen coming on during the night, almost constant vomiting for forty-eight hours, and marked diarrhœa, with tenesmus. The prostration must have been pronounced. This disturbance was apparently due to eating ice-cream and drinking considerable beer later. He now began to have frequent attacks of gastric disturbance, and he says "his stomach has not been right since." As a rule, anorexia, rarely vomiting, but considerable gastralgia have been persistent symptoms during the last year or more. The extreme pallor was first noted one year ago and has been gradually increasing. The patient was treated six months ago in Greensborough, North Carolina, and thinks he was given quinine, arsenic, and iron. He thinks he has had some little fever at intervals. He improved for a time, but six weeks ago he decided to visit relatives in Baltimore, as he realized his disease was taking a serious course. The journey north tired him a great deal, and he almost fainted in the station here, and in Washington he was obliged to take whiskey at short intervals. His friends here were shocked at his appearance. He was treated by a physician, who pronounced the case cancer of the stomach, and advised operation. As a medical student was living in the house in whose ability the people had confidence, they asked his opinion about the case, and, as he differed from the former diagnosis, I saw the case as a third party.

Notes at Bedside. A man of large frame, looks older than forty-six years. Extremely anæmic tongue, lips and finger-nails show extreme pallor. He is still fairly nourished, but signs of loss of flesh apparent. The skin in general has a dirty, very light lemon color; this is more marked over lower abdomen and the face. Hair is gray and very dry. Breath bad. Several decayed teeth, especially the left first molar. No pus apparent about the teeth. Tongue coated slightly, thickened, but not tender. No subcutaneous hemorrhages. Lungs clear on auscultation and percussion. Heart impulse just in nipple line; soft blowing systolic murmur over body of heart, not transmitted to right or left. Liver not enlarged, not tender. Abdomen in general looks natural. Stomach area about normal on percussion. Deep pressure in epigastrium gives rise to some pain, and the patient is immediately nauseated. Slight cedema over dorsum of the feet and over ankles. Both patellar reflexes are abolished; the plantar reflexes are still present. No apparent atrophy of any group of muscles. No sensory disturbance elicited; feels heat and cold everywhere. When asked to walk there is no difficulty apparent. There is, however, considerable Romberg symptom present. When the patient attempts with eyes closed to touch the knees with the heel of the opposite foot he comes rather wide from the mark, and there is a slight ataxic swaying of the extremity. It is difficult to say if this is a true ataxia, as the extreme muscular weakness might account for it. No bladder or rectal disturbance. Vision good.

Ophthalmoscopic examination shows two punctiform hemorrhages in the right eye in the lower quadrant of the fundus and a small hemorrhage just at the edge of the disk in the left eye. No nystagmus.

Pupils react to light and accommodation.



Blood Examination. 1,800,000 erythrocytes, 7000 leukocytes, and 22 per cent. hæmoglobin. Specimens were stained after drying on copper plate and also after fixing in absolute alcohol and ether. Specimens show a marked poikilocytosis; almost every corpuscle is distorted. Many microcytes and a few macrocytes and about forty nucleated red blood cells were found in a blood smear. The first specimen showed no megaloblasts; the second, which was examined with the sliding stage, showed six. They were typical. Urine contains a trace of albumin; specific gravity, 1016. No casts; no diazo-

The patient was seen four or five times, but I made only two personal blood examinations, and, as my student friend had little opportunity to carry these out, my report is rather incomplete.

When last seen the blood count had improved slightly, 2,000,000, but there are several megalocytes now seen in the stained specimen, February 11, 1902. The patient died on March 2, 1902, from bronchopneumonia.

A complete autopsy was not granted, and I was only allowed to remove the cord, and this was not an easy matter in a private home.

Description of Cord. No macroscopic changes evident; meninges normal.

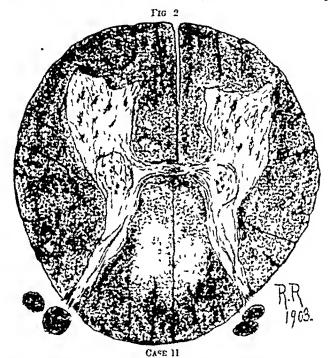
Description of Microscopic Changes Found in the Spinal Cord in Case I. Small pieces from every portion of the cord and medulla were placed in formalin and in a mixture of Müller's fluid and formalin. After hardening they were stained by the Weigert, Weigert-Pal, Van Gieson, and eosin and hæmatoxylin methods. In this case the Marehi stain was not employed. In every specimen examined, no matter what the staining method was, it was quite evident that a narrow strip of degeneration was present in both the column of Goll and that of Burdach, most marked in the former in most sections. The degeneration was most apparent in the lower cervical and upper dorsal regions. The drawings from this ease were made from specimens stained by the Weigert-Pal staining method, and the blanched area in the posterior tracts of the cord represents the degenerated fibres. In the Van Gieson specimens it was clearly shown that these degenerated fibres had lost their myelin sheaths, and very few axis-cylinders could be made out in the degenerated areas. The remainder of the cord was absolutely normal. There were no hemorrhages found; the bloodvessels were normal, as were also the meninges. In all sections examined the same degeneration was apparent as far down as the upper sacral cord.

Case II.—This case is of special interest, I think, in that the spinal symptoms seemed to precede the onset of the anemia. Mrs. M., seen in November, 1902, aged thirty-four years; mother of two children, and who has had two stillbirths; the last child was born when seven months old, in 1900. Family history negative, except that one maternal uncle died of phthisis. She has had scarlet fever and measles. Typhoid fever at twenty years. No sequelæ. Has been of a neurotic disposition, and for several weeks during her first pregnancy was quite hysterical. No history of syphilis or its

secondary manifestations.

She dates her present trouble to her last pregnancy, which resulted in a miscarriage at the seventh month of gestation, in 1900. She had fever for three weeks after this, and was a very siek woman. No marked rigor, but chilly feelings. Some muscular pains, but these were not marked. No swelling of the joints. After spending seven weeks in bed she was allowed to sit up, but was too weak to walk, even about the room. She has always had a rather sallow complexion, but has generally weighed between 130 and 135 pounds. In the early part of 1901 the patient was still run down, but was able

to attend to light household duties. About this time she noticed a peeuliar feeling and sensation of cold in the right thigh; this was especially marked when fatigned. Later a very similar sensation was noticed in the left thigh, but more over the buttocks. At times she had a feeling as though hot water was being poured over her lower extremities. This was nothing that troubled her. In August, 1901, she was in a driving accident, which left her very nervous, and she was subject to erying spells and suffered with pain down the back, and she seemed to have slight difficulty in walking, especially in the dark. No lancinating pains, but she still felt the sensations described above. She began to suffer with her stomach, and had constant feelings of weight in the epigastrium, and the pressure



of elothing was very annoying. She did not vomit, but was frequently nauscated, especially in the morning. At this time she began to get pale. She took iron and quinine, probably arsenic, but her anæmia, except with periods of improvement, has steadily increased.

Notes at Bedside. A moderately well-nonrished woman; subcutaneous fat well preserved. She is extremely pale, and the skin has a faint suggestion of a yellow tinge. Tougue coated and rather sensitive to pressure and feels hard and is somewhat thickened, espepecially the anterior two-thirds. Teeth in fairly good condition. No glandular enlargement. Hair very dry and without lustre; not gray. Lungs clear throughout, except a few moist râles at the left base. Heart: A very loud hæmic murmur over the base, which is

transmitted to the vessels of the neck. Apex-beat about the nipple line. Liver slightly below the costal border, 3 cm. Stomach is also displaced downward. The right kidney is readily palpable and slightly movable; in fact, a moderate degree of Glénard's enteroptosis exists. Test meal shows trace of hydrochloric acid. No lactic acid. Motor function of stomach evidently sluggish and some hypersecretion present.

Blood Count. 2,000,000 erythrocytes, 9000 leukocytes, and 32 per cent. hæmoglobin. Stained specimen with Ehrlich's triple stain shows marked poikilocytosis. Microcytes numerous; also macrocytes in several fields; and in about every fourth or fifth field an atypical megaloblast is visible, with very dark nucleus. Beautiful karyokinetic figures are seen in some of the nucleated corpuscles, and several erythrocytes show the polychromatophilic degeneration.

Examination of Nervous System. Gait is rather stiff, but no typical ataxia when the eyes are open. She watches the floor very intently. With closed eyes there is evidently a slight ataxia. Well-marked Romberg symptom. Both patellar reflexes absent. Plantar reflex present. No Babinsky reflex. No atrophy of any muscles. Apparently a slight dulling to the differentiation of heat and cold over the right thigh, but this is slight. Touch normal. No other sensory disturbance; patient says she is rarely free lately of the paræsthetic sensations in the lower extremities. No lancinating pains present. Has never noticed any bladder or rectal symptoms. Patient seen on one more occasion, and this was two weeks before her death, which occurred in January, 1903. Post-mortem limited to removal of cord and brain and inspection of abdominal viscera, which could not, however, be removed.

Cord. Macroscopic appearance normal.

Description of Microscopic Examination of Cord from Case II .-The entire cord was removed and sections from all regions placed in formalin, Müller's fluid with formalin added, also a few sections stained by the Marchi method, besides Van Gieson and eosin and hæmatoxylin staining. In all sections from whatever regions of the cord, except the very lower dorsal, ninth to the twelfth segments, and the sacral portion, a well-marked degeneration, involving almost the entire posterior tract of fibres, including the columns of Goll and Burdach. In this, as in the former case, the change was most pronounced in the upper dorsal and lower cervical regions. With the Weigert-Pal method a slight blanching of both right and left lateral columns was evident, but it was only after using the Marchi stain that it became evident that a considerable number of nerve fibres had degenerated in these lateral areas, this degeneration being probably of recent date. The anterior portion of the cord was normal. No hemorrhage found. The bloodvessels, nerve cells, and meninges were apparently normal. Nissl's stain was not employed, so one can say nothing in regard to the nerve cells, except that they showed no marked shrinkage.

In this case the reader will remember that there was evidence of property of a remain for several months: in REULING: PERNICIOUS ANÆMIA.

spinal disease preceding the onset of anemia for several months; in the pronounced paramethorine rather diminished toward the and spinal disease preceding the onset of ancimal for several months; in fact, the pronounced paraesthesias rather diminished toward the of the disease. ract, the pronounced paraestnesias rather annumence toward the city of the disease.

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in permenous ancients, one maying a preduction for causing degenera-tive changes in the red blood cells, while the other seems to have a The theory that these degenerations start from hemorrhagic focispecial affinity to the spinal cord fibres.

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CASE III.—A male aged forty-eight years; married; born in the Case when to work old who come is the United States when the work old when the work of the Case when the work old when the work of the Case when the C Bohemia, but came to the United States when ten years old.

The Bohemia, but came to the United States when the Property Character and the Property Character and the Condition of the Condition cord from this case was kindly given me by Dr. Flexner. the outoner was admitted to the Johns Honkins Homital in 1001. cord from this case was kindly given me by 17r. Flexher. The patient was admitted to the Johns Hopkins Hospital in 1901; the autopsy was performed at the bostiful Tinfortunately Lean only present a performed at the bostiful was admined to the Johns Hopkins Hospital in 1901; the autopsy was performed at the hospital.

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the history in full; these notes were taken from the history when the the mistory in this; these notes were taken from the history which the cord was obtained. The patient complained of extreme weakness, and vertice the companion has been a coal-miner. cord was obtained. The patient companied of extreme weithness, breathlessness, and vertigo. His occupation has been a coal-miner, breathlessness, and vertigo. preamessness, and verago. This occupation has been a confinite, about the mines since his boyhood.

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the patient attributes has present timess to stomach trouble, ne being fully convinced he has cancer of the stomach, which he being fully convinced he has cancer of the stomach, which had the being fully convinced he has cancer of the stomach had the being fully convinced he has cancer of the stomach had the stomach being may convinced he has cancer of the sounder, which he belly.

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excused at the time and was mad up for about two weeks.

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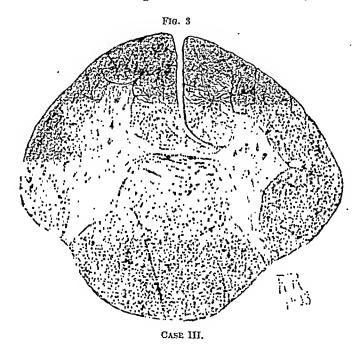
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Description of the Pathological Changes in Case III. The same are proposed in the good from this case as in a pathods were evaluated in the good from the case.

staining methods were employed in the cord from this case as in Case I the Varehi method not being used. Case I., the Marchi method not being used.

The only change from the varieties method not being used.

The pormal are coveral small circumcaribed areas of degeneration the normal are coveral small circumcaribed. the normal are several small circumscribed areas of degeneration, which are readily seen under the lowest power of the microscope; these were limited to the anterior parts of the cord. On closer examination it is evident that these degenerated fibres were caused by small hemorrhages into the cord substance. Several were found in the upper sacral region, as shown in the illustration, and two well-marked hemorrhages in the dorsal region between the third and fifth segments. In these the presence of blood pigment is clearly seen, and it easily explains why they should occur in the anterior portion of the cord, this being the most vascular portion. In this case the posterior and lateral columns are absolutely normal. As to the cause of these hemorrhages, they are no doubt due to some changes in the coats of the smaller vessels, very likely a form of hyaline degeneration; no doubt the effect of the unknown toxin, which seems to be the ctiological factor in this most perplexing dis-



case. That such degenerations are not found in the ordinary secondary anæmias, even the most severe cases, as those seen after infection with the bothriocephalus, etc., this is well shown in the cases and pathological report of Minnich and Nome on cases of pernicious and secondary anæmias. Lichtheim was the first to call attention to the tabetic-like changes in the spinal cord in pernicious anæmia. In this country the most important article on the spinal changes in this disease is that of Putnam, who also reports several cases in which well-marked spinal symptoms, mostly of a tabetic character, with paræsthetic sensations, preceded the onset of the pernicious anæmia. The reader is also referred to articles of Goldscheider, Nome, Marie, Turner, Minor, and Grasset.

# A HUMAN EMBRYONIC VESICLE SHOWING EARLY · PLACENTA FORMATION.

BY JOHN M. SWAN, M.D., PATHOLOGIST TO ST. MARY'S HOSPITAL, PHILADELPHIA.

(From the Pathological Laboratory of St. Mary's Hospital.)

THE specimen from which the sections exhibited were taken was given to me in the laboratory of St. Mary's Hospital in June, 1903, by Dr. D. F. Harbridge. It had been passed from the vagina of one of his patients about June 16th. After the passage of the specimen the patient had profuse hemorrhage for a week, and had fainted on account of the loss of blood.

On November 17, 1902, the woman had been in a trolley accident, and six days later she had a miscarriage. The product of conception was estimated by Dr. Harbridge to be between the sixth week and the second month of development. Since this miscarriage the patient's menstrual periods had been irregular and the flow had been profuse.

The specimen was a spherical, fleshy mass, brown in color, about 0.5 cm. in diameter. On section it was found to contain a cavity, which was lined by a membrane that resembled amnion in appear-

ance.

Microscopically this membrane proved to be chorion, with its villi projecting into the maternal blood spaces and bathed in the maternal blood. The villi are seen to be composed of fetal mesoderm, which is limited by two layers of tissue: first, a layer of distinctly outlined columnar cells, each containing an oval nucleus; and second, a continuous layer of cytoplasm containing irregular nuclei, but showing no demarcation into cell areas. The former of these layers, known as the layer of Langhans, is formed of the fetal ectoblastic cells, which are the remains of the trophoblast; and the latter is the syncytium, a descendant of the trophoblast.

The tissue at the periphery of the section is the decidua placen-

talis, and shows the dilated vessels which ramify in it.

The earliest recorded human placenta that has been examined is that described by H. Peters, of Vienna, in 1899. The following is a brief résumé of Peters' conclusions, after studying the appearances of the developing embryonic vesiele, which he estimated to be four

days' old:

By the time the impregnated ovum reaches the uterine cavity it is surrounded by a chorion, which is covered on its free surface by epithelial cells of ectoblastic origin. The embryonic vesicle is lodged in a fold of the decidua, and, by a process of erosion, eats its way into the stroma of that membrane, the point of entrance of the embryonic vesicle into the stroma of the decidua being marked by

a blood clot. In this way the decidua placentalis is produced between the museular wall of the uterus and the embryonic vesicle, and the decidua capsularis is produced between the embryonic vesicle and the eavity of the uterus.

The epithelium of the chorion proliferates and forms a dense mass of cells known as the trophoblast, which presents villous projections, with intervillous spaces. The villi grow into the decidua placentalis and become attached to the deeper layers of that tissue or to the



Section of young human placenta. a. Decidua placentalis. b. Chorionic villi in cross-section. c. Chorionic villi in iongitudinal section. d. Chorion. e. Maternal blood space. f. Mesodermic core of chorionic villus g. Red blood corpuscles in maternal blood spaces. h. Layer of Langhans. i. Syncytium.

muscular wall of the uterus, coming in relation as they grow with the dilated decidual capillaries. By phagocytic action the cells of the trophoblast absorb the endothelial lining of these capillaries, allowing their contained blood to lie between the projecting villi. The villi, at first simple, subsequently become branched, the branches lying free in the decidual blood spaces. Coincidently with these changes, the chorionic mesoderm becomes vascularized by the ingrowth and extension of the allantoic bloodvessels, by which means the fetal blood is carried into the chorionic villi in close relation with the maternal blood spaces. The maternal blood on the one side and the fetal blood on the other side absorb the cells of the trophoblast until only two layers are left, the layer of Langhans and the syncytium. In the future development the former layer is absorbed so that in the placenta at term the syncytium is all that remains of the original ectoblastic covering of the chorion. Then the fetal blood is separated from the maternal blood by the syncytium, the interposed mesoderm of the villus, and the endothelium of the fetal capillaries.

# REVIEWS.

Introduction to the Study of Malarial Diseases. By Reinhold Ruge. Translated by P. Edgar and M. Eden Paul. London: Rebman, Limited, 1903.

In spite of its modest title this book represents a fairly comprehensive exposition of the subject and strikingly shows the direct application of scientific research work to practical questions of hygiene and practice. This is brought out very clearly in the chapters on Epidemiology, on Therapeutics, and on Prophylaxis, which ought to be carefully read and assimilated by everyone engaged in medical education, whether in the narrower sense of lecture-hall and clinic-room instruction, or in the sense of education of the public. In the first—the choice of chapter headings is not altogether a happy one—which deals with the origin of malaria, there is brought forward such an array of convincing arguments in support of the theory of the dissemination of malaria by mosquitoes and a refutation of the objections that have been urged against it as to sweep

the last vestige of doubt from the most skeptical mind.

The treatment of malaria obviously resolves itself into the proper method of administering the sovercign drug, quininc, and on this subject the author's ideas are quite definite, if somewhat radical. Briefly stated, his directions for the administration of quinine in benign (tertian and quartan) intermittent fever are to give "one gram or fifteen grains of quinine four or five hours before the impending paroxysm, and repeat this dose at the same hour every day for six successive days." He believes that fifteen grains is the minimum dose for an adult if the blood is to contain a quantity of quinine sufficient to be effective against the parasite. The same large dose is therefore required when quinine is given to control the fever permanently or as a prophylactic measure, for both of which objects it is to be prescribed on two successive days at intervals of ten days, for he has ascertained that two successive doses of quinine have a more powerful effect than one isolated dose. This periodic administration of quinine, corresponding to our "tonic" dosing, is to be kept up for three months after the disappearance of the paroxysms and of the fever, even when the patient has removed to a region where he is no longer exposed to fresh infection. With regard to the method of administration Ruge arbitrarily condemns all but the drug in solution or in wafers; "tabloids" especially are treated with utter contempt. The reader will bear in mind, however, that the book is written by a naval surgeon and primarily for the use of naval and military surgeons, who are less bound by prejudices and traditions than any other class of practitioners. Incidentally it is also written by a German, and the writer's national pride asserts itself in the liberal references to Koch, who, it would appear, according to the author, has done most, if not all, the recent important work on malaria. The latter's method of prophylaxis, consisting in the hunting down and curing with quinine of every individual case of malaria, especially the slight eases which are ordinarily overlooked, and the cases of relapse which keep up the disease during the off season, is the one that seems to the author to be the most effective, supplemented by personal prophylaxis. Methylene blue is the only drug that is capable of taking the place of quinine and, accordingly, finds its chief use in the treatment of black-water fever.

The author, with an implied apology, devotes a great deal of space in the chapter on Diagnosis to a description of the technique of making blood preparations, as "good preparations are, above all, needed for the successful demonstration of malaria parasites." His methods differ in a number of points from those usually employed; thus he obtains the blood neither from the tip of the finger nor from the lobe of the ear, but prefers "the back of one of the ungual phalanges," where the prick is less painful and the skin is thinner, so that the drop appears almost immediately. For spreading the film the ingenious method of Jancso and Rosenberger is advised, by which an even film of the desired thinness is obtained and the blood is spread without the least pressure, thus preserving the morphological integrity of the corpuseles.

R. M. G.

ATLAS OF THE EXTERNAL DISEASES OF THE EYE. INCLUDING A BRIEF TREATISE ON THE PATHOLOGY AND TREATMENT. By PROF. DR. O. HAAB, of Zurich. Authorized Translation from the German. Second edition, revised. Edited by G. E. DE SCHWEINITZ, A.M., M.D., Professor of Ophthalmology in the University of Pennsylvania; Consulting Ophthalmic Surgeon to the Philadelphia Polyelinic; Ophthalmic Surgeon to the Philadelphia Hospital; Ophthalmologist to the Orthopedic Hospital and Infirmary for Nervous Diseases. With 98 colored lithographic illustrations on 48 plates. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

THESE plates and descriptions with the companion volume upon the fundus are of inestimable value in the study and practice of ophthalmology. They replace, as far as may be, the clinic and instructor. Their low price and convenient form must cause them 532 REVIEWS.

to supplant the larger plates. Practically all discase forms of the external and internal affections of the eye are portrayed in colors with full and clear descriptions in the text, including symptomatology, etiology, and treatment. Quite naturally all the plates are not of the same excellence, but no serious objection can be brought against any, and some are superb.

From considerable familiarity with the German edition, we have no hesitation in saying that the present descriptions in English (the plates are the same) are superior to the original in clearness, terseness, and ease of style. In this case it is not true that traditore is

tradutore.

Of the comments added by the editor, Prof. de Schweinitz, we can only say that we wish there were more. They are valuable addenda, and occasionally rectify certain special views somewhat peculiar to the author.

The two volumes form a companion set which can with advantage be in the hands of every practitioner, even though he be not a specialist.

T. B. S.

International Clinics. Edited by A. O. J. Kelly, A.M., M.D., Philadelphia, Pa. Vol. III., pp. 305. Thirteenth series. Philadelphia: J. B. Lippincott Co., 1903.

THE present volume opens with an excellent series of papers on "Diseases of the Gall-bladder and Gall-ducts." Musser discusses the medical aspects-some medical aspects, as he terms it-first presenting a skeleton, which he subsequently clothes with very substantial flesh, while Rudolph presents the "Causation, Symptoms, and Diagnosis of Gallstones." Stockton broadens the subject with his "Diagnosis and Medical Treatment of Cholelithiasis and Cholecystitis," while the surgical aspect of the case, so far as regards the indications and value of intervention, falls to Lejars. Deaver, on the "Surgical and Postoperative Treatment of Chronic Gallstone Disease," extends the subject. The symposium is completed by Weber, on "Biliary Cirrhosis of the Liver with and without Cholelithiasis." In the first place, it is apparent that in gallstones we have neither the beginning nor yet the end of the gallstone disease; further, that pathology and particular pathological findings, as shown by surgery, teach us that there is a medical aspect which is not to be ignored; and, finally, a careful diagnosis is essential and a working diagnosis possible in the great majority of eases. To one who wishes to know the present status of the gallstone question we can refer this volume, wherein a most satisfactory presentation is found. The one hundred and twenty pages constitute a veritable monograph.

Treatment is well represented by Finlay on "Pneumonia," Robin

on "Gastric Cancer," Rose on "Carbonic Acid in Rectal Disease"—presumably meaning carbon dioxide gas—and Chantemesse on "Typhoid Fever Serum;" all good. Medicine is not far in the rear with Craig on "Malarial Infections," which clears the atmosphere; Leslie on "Clinical Types of Pneumonia," suggestive even to one whose experience has been so ample that he is alert for surprises; Mays on "Sudden Death Due to Respiratory Disorder" invoked the nervous system as an explanation, a paper for thought; Fowler writes on an "Intermediate Type of Leukæmia," as though we had not enough unsettled questions without the addition of another, and finally Poynton on the "Clinical Evidence of Myocardial Damage in Rheumatic Fever." With this valuable series of important papers surgery seems accorded hardly enough space. Bodine on "Cocaine Anæsthesia in Operation for Varicocele," Lewis on "General Anæsthesia," Lucas-Championnière on "Asepsis and Antisepsis," Rodman on "Gastrostomy; Concussion of the Brain," and Belfield, with a practical paper on "Intrascrotal Tumors," gives in small compass much valuable information, and Schwartz closes with the "Modern Treatment of Varicose Veins."

We have had in the past, at times, some misgivings as to the scope of this series. It seems to be intermediate between the journal and the monograph. In the past there have been volumes whose contents properly belonged to ephemeral journalism and the papers were tardy. At others an effort has apparently been made to cover too much ground. Again we have found articles which were almost monographs in their completeness. We believe the present volume meets our ideas. What has been selected has been thoroughly and ably done. The gallstone question in this volume, taken by itself, is notable and there is plenty more for good measure. May the editor continue to have the energy to draw out brilliant papers and the discrimination to properly group them!

R. W. W.

THE DECENNIAL PUBLICATIONS. THE DISTRIBUTION OF BLOOD-VESSELS IN THE LABYRINTH OF THE EAR OF SUS SCROFA DOMES-TICUS. By GEORGE E. SHAMBAUGH, M.D. Chicago: The University of Chicago Press, 1903.

Dr. Shambaugh's monograph is a model of its kind. The work was undertaken for the purpose of studying the vascular supply in the labyrinth of the ear. A satisfactory study of the vessels in the adult is almost impossible, owing to their complexity, therefore the author was led to take up the study in the embryo. The difficulty of such a study may be realized from the fact that out of five hundred embryos injected only about one hundred of the specimens were found suitable for the study. The author describes carefully the methods which he employed, chiefly that of Eichler, which

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consists in making celloidin casts of the labyrinth, from preparations in which the bloodvessels had been previously injected. The methods used are described in full. A special feature of the monograph, however, will be found in the excellently colored plates. These are drawn with such evident accuracy that even if accompanied by a very slight text, they clueidate perfectly the points which the author brings out. On the whole, Dr. Shambaugh's study does not contain any startling anatomical find, but it does establish the anatomy of the circulation of the labyrinth on a definite basis, and therefore possesses the greatest value. F. R. P.

THE MEDICAL NEWS VISITING LIST, 1904. Philadelphia and New York: Lea Brothers & Co.

THE PHYSICIANS' VISITING LIST FOR 1904. Philadelphia: P. Blakiston's Son & Co.

BOOKS of this kind are an invaluable adjunct to the physician and his work, and the two under consideration are so well known to the medical profession that their characteristics need hardly be described. Some systematic form of record of visits, vaccinations, births, etc., is absolutely necessary to those engaged in practice. Both the Medical News and the Physicians' List have enjoyed continuous popularity with the profession for many years. Their general get-up and plan is the outgrowth of an intimate need of what is necessary in such volumes, and it is not likely that, having maintained their popular favor all these years, there can be found any plan to improve upon their scheme.

J. H. G.

A TREATISE ON ORGANIC NERVOUS DISEASES. By M. ALLEN STARR, M.D., Ph.D., LL.D., Professor of Diseases of the Mind and Nervous System in the College of Physicians and Surgeons. New York and Philadelphia: Lea Brothers & Co., 1903.

The specialty of diseases of the nervous system has not, in late years at least, suffered from any lack of exposition of the subject through text-books and extensive monographs. There is, however, and always will be, a demand by the profession for text-books which embody the advance of knowledge in any particular line of work, with the basic and established principles. The text-book under discussion will be accepted by the profession in general, and neurologists in particular, as an example of a concise, clear-cut, complete presentation of an especially difficult and intricate subject. There has undoubtedly been a remarkable advance in our knowledge of

the central nervous system and its diseases in recent years. The increase in the literature is out of all proportion to this advance. This is due in the main to single case reports and the tendency to individualize cases of a particular disease group, both from a clinical and pathological standpoint, has not only overburdened the literature of the subject, but has blurred the sharp outlines of the disease types to which we are accustomed in other branches of medicine. result of all this is that the exposition of such a subject in order to be complete, and at the same time within convenient bounds, implies an ability for condensation, systematization, and digestion on the part of the author far beyond that called for in any other What Oppenheim has done for the German student Starr has succeeded in doing for the English, and much after the same method. The condensation and digestion is well carried out by means of footnotes, with references to the original articles, a distinct advantage over that of other works, where only the names of the investigators are given.

The personal element is strongly marked throughout the book. The author has drawn freely from his long and extensive practice in illustrating the different types of disease by the addition of case records, photographs, etc. Many of the sections illustrating diseased conditions are from his own cases and others from other American investigators, although a large number of these illustrations—i. e., of the pathology—are drawn from the standard foreign works. In treatment the book is especially good, and here again, as in prognosis, long years of experience has lent that proper perspective to the value of methods and drugs and their results. Many of the elapters—Tabes, Anterior Poliomyelitis, Peripheral Neuritis—might be considered as monographs rather than chapters of a text-

book.

The pathology of the different diseases is carefully considered and well illustrated by drawings and photomicrographs, as noted Sufficient attention, however, is not given at times to accuracy in the use of technical terms. The term neuron, quite needlessly, is used in a confused way to express the whole or part of the neuron. The posterolateral scleroses, both in the clinical and pathological descriptions, are insufficiently treated. The term sclerosis is used for the diffuse degenerations and no differentiation attempted. Putnam is given the credit of being the sole observer as to the different stages, etc., of the disease—i. e., distinguishing between symptoms of long and short standing in the same case. That tumors of the pituitary are usually fibroma or myxoma will not be accepted by those who have studied the pathology of this gland carefully. These, however, are minor errors, which one may pick out of such a work easily enough, but have little influence in the estimation of its real value.

There is considerable room for improvement in the indexing,

reference of some authorities, and correction of typographical errors. The book itself is of 750 pages; the 275 engravings in the text and the 26 plates are very well executed and add greatly to its value. The paper is good and the printing and binding all that one might wish for. Altogether the book is a credit to American neurology, and will compare favorably with the standard text-books of other languages.

D. J. McC.

RECHERCHES CLINIQUES ET THERAPEUTIQUES SUR L'EPILEPSIE, L'HYSTERIE, ET L'IDIOTIE. Volume XXI. Compte-rendu du service des enfants idiots, épileptiques, et arriérés de Bicêtre pendant l'année 1901. Par BOURNEVILLE. Paris: Félix Aleon, 1902.

Trus volume is more of an annual report of the department for epilepsy and idiocy of the Bicetre than a volume of research, as its title would indicate. Over half the volume is concerned with a statistical study of the number of patients, movement of population, history of the service, etc. Then follow ten contributions to the study of idioey and epilepsy by Bonrneville and his assistants. The effect of bromide of camphor in epilepsy is studied with apparently favorable results, and is quite up to the standard of the clinical studies of the best French clinicians. The other articles, all original investigations, are as follows: "A Study of Puberty," by Bourneville; "A Contribution to the Study of Moral Idiocy, with Especial Reference to Lying as a Symptom," by Bourneville and Boyer; "A Study of the Relation of 'Museular Impotence' and Bony Deformities in Infantile Hemiplegia," by Bourneville and Bangour; "Hemorrhages of the Skin and Mucous Membranes after Epileptic Attacks," by Bourneville; "Symptomatic Idioey Due to an Atrophie Sclerosis of the Right Cerebral Hemisphere," by Bourneville and Crouzon; "Idioey of the Mongolian Type," by Bourneville, and also another article on the same subject by Phillipe and Oberthur; "True Porencephaly and Pseudoporencephaly," by Bourneville and Morel. The titles indicate the substance of the articles given. They constitute a valuable addition to the pathology of idiocy.

A study of the schools for backward children will be of interest to those laboring with this difficult problem. D. J. McC.

Nose and Throat Work for the General Practitioner. By George L. Richards, M.D. NewYork: International Journal of Surgery Company, 1903.

This little work is really a novelty in its own particular line, and its author is to be congratulated upon the most excellent way in which he has fulfilled the object which he intended to accomplish.

It is based throughout on his own extensive personal experience,

and it is this which gives the keynote to the volume.

While giving the diagnosis and treatment of morbid conditions in the nose and throat, as they fall within the province of the general practitioner, Dr. Richards is careful to indicate the difficulties which confront those who are not especially skilled in rhinology and laryngology, and thus not lead them into attempts to do that which does not lie within their province. The book is not only adapted to the general practitioner, but will prove an especially useful guide to those who desire to take up laryngology and rhinology as special pursuits. It is in no sense of the word a compend, nor does it pretend to furnish a complete text-book. Dr. Richards writes in a clear style, admirably suited to his subject-matter. This book is a pioneer in its line and deserves the professional favor with which it is sure to be received.

A NARRATIVE OF MEDICINE IN AMERICA. By JAMES GREGORY MUMFORD, M.D. Philadelphia and London: J. B. Lippincott Co., 1903.

This work covers the entire field of the history of medicine in America from the earliest time down to the present date. Its title has been well chosen by the author, who has given us what is truly a story or narrative of the medical profession rather than a dry series of historical facts. Within recent years there has been a great impetus given to the study of medical history, and much has been written upon it. Dr. Mumford has not only availed himself of the work which has been done in this field of investigation by others, but has gone to original sources and has authenticated or

disproved many disputed statements.

In a book of this character it is most difficult to observe a proper proportion in dealing with various epochs or individuals, and its author is to be congratulated upon the skilfulness which he has shown in weaving the network of his narrative. Beginning with the early days of settlement, when the sick and injured depended for relief upon the amateur medical attentions of pastors or deacons, like Samuel Fuller, Dr. Mumford goes on to the real beginnings . of medical history in this country, when bright young men who determined to practise medicine sought their knowledge at the feet of the best teachers in England and on the Continent, and brought back to this country the lessons which they had learned from the Hunters, Haller, Boerhaave, or Morgagni. Most interesting are his accounts of the carcers of the founders of American medicine: Morgan, Shippen, Rush, and John Jones—each skilfully delineated, with the estimates of their characters and accounts of their mutual relations given. Coming to a later date, when medical science had

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extended from Philadelphia, Boston, and New York, penetrating other sections of the country, Dr. Mumford describes most sympathetically and graphically the great services rendered by pioneers, such as Drake and Dudley. In fact, among the most interesting portions of the book will be found those devoted to the careers of these men, many of whom figure to the present generation as names and naught else.

Although Dr. Mumford pays due attention to the founding of hospitals and medical schools, and describes the services of men like those above mentioned and the Warrens of Boston in this connection, we doubt if the histories of institutions will ever thrill us as do the life-histories of men who struggled through almost insuperable difficulties to the achievement of such tremendous benefits to humanity.

Dr. Mumford's book should not only be read but owned by every American physician, and we could think of no more stimulating gift to be put in the hands of the graduate than this narrative, in which are embodied the wonderful achievements of his predecessors in the healing art.

F. R. P.

PRACTICAL POINTS IN NURSING. For Nurses in Private Practice. By EMILY A. M. STONEY. Third edition. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

THE third edition of this valuable book on nursing has been revised and brought up to date by a physician owing to the death of the able author.

The work itself, except for the revision made necessary by advance in knowledge, retains much of its originality. The authoress was peculiarly qualified by experience and position to write authoritatively, and she is to be doubly commended for omitting much that a nurse need not know, as well as for the good selection of what she should know.

The matter has been divided into seven chapters and an appendix: I. The Nurse; II. The Siek-room; III. The Patient; IV. Nursing in Accidents and Emergeneies; V. Nursing in Special Medical Cases; VI. Nursing of Sick Children; VII. Physiology and Descriptive Anatomy. The appendix contains various kinds of useful knowledge, such as tables of weights and measures, recipes, dose list, glossary, etc. The difficulty in instructing nurses lies in knowing just how much to teach and how much to withhold. It is necessary for the modern trained nurse to have an intelligent knowledge of the reason for pursuing a particular course or abandoning another. It is not necessary, on the other hand, for a nurse to take a complete medical course. Miss Stoney's work contains many things of interest to

physicians as well as to nurses, and should prove a valuable aid for nurses in their private work. The book has its need also, as private nursing is somewhat different from hospital work, and often a nurse is at a loss for many kinds of information not picked up at the hospital.

J. N. H.

A Manual of Plague. By William Ernest Jennings, M.B., C.M., Major in the Indian Medical Service; Chief Medical Officer for Plague Operations in the Bombay Presidency, etc. With an Introduction by Surgeon-General G. Bainbridge, M.D., M.R.C.P., I.M.S. London: Rebman, 1903.

THE extensive and really alarming outbreak of plague which but a few years ago threatened to spread from the East to Occidental nations has drawn particular attention to the study of this disease; and so important and numerous have been the discoveries concerning its etiology, treatment, and prophylaxis that a thorough exposition of the present knowledge concerning the subject can scarcely be gained from the ordinary text-book of medicine. In certain countries where plague is likely to occur it is absolutely necessary that the practitioner should be thoroughly conversant with every aspect of the disease. To this end the present manual is excellently adapted, for it treats of the subject from a practical standpoint, and is besides essentially up to date. The book opens with an introductory chapter upon the interesting history of plague epidemics, after which follow chapters on the bacteriology, pathology, treatment, epidemiology, symptomatology, etiology, etc. The diagnosis and prognosis are appropriately treated and many important pages deal with measures for the suppression and prevention of the spread of plague. The author's personal knowledge and extensive experience with the disease certainly give the book a practical value.

There are a number of illustrations, most of which are fairly good. The book is well printed and nicely bound. W. T. L.

A Manual of Hygiene and Sanitation. By Seneca Egbert, A.M., M.D. Third edition, enlarged and thoroughly revised. Philadelphia and New York: Lea Brothers & Co.

THE third edition of Dr. Egbert's very useful manual shows evidence of very careful and thorough revision of every chapter. New material and numerous additional illustrations have been introduced where needed. Disinfection has been divorced from Quarantine and placed in a chapter by itself, and the chapter on Laboratory Tests has been much improved. The first edition was

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a valuable addition to the literature of Hygiene, the second was an improvement over the first, and the third is better than the second. As the author keeps his work abreast of the times, each revision eauses an increase in size; and it seems probable that before long he will have to determine where a cut can be made with least injury to the book as a whole. It is the opinion of the reviewer that the chapter on Bacteriology could well be spared even now, for it is slight and sketchy; it can be of no assistance to those who have had an elementary course in the subject, and is not full enough for those who have not. Moreover, a work on Hygiene should no more include elementary bacteriology than elementary physics, chemistry, or mathematics.

C. H.

Modern Surgery: General and Operative. By John Chalmers Da Costa, M.D., Professor of Principles of Surgery and of Clinical Surgery, Jefferson Medical College, Philadelphia; Surgeon to the Philadelphia Hospital and to St. Joseph's Hospital, Philadelphia. Fourth edition, rewritten and enlarged, with 707 illustrations, some of them in colors. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

ALTHOUGH the whole science of medicine is constantly and steadily progressing, perhaps the most noted advances are in the realm of surgery, where new methods, improved technique, and more modern patterns of instruments are ever pressing the old ones into the background. For this reason a text-book on surgery very soon becomes out of date unless continually revised and rewritten, for, though many of the procedures have come to be regarded as standard ones, student and practitioner alike will not be satisfied with a work containing these only, but demand methods of the day and hour, such as the Lorenz treatment and others of a kindred nature. this aspect Da Costa's Surgery is excellent. This fourth edition has continued the many good points of the previous editions, but has been entirely rewritten, many procedures now obsolete having been dropped and their places taken by modern methods. It is not a large work, the general divisions corresponding to the generally accepted classification of subjects in all standard works on surgery. The discussions, both in regard to Symptomatology and Treatment, are brief but clear and concise and well adapted to teach what the author wishes. A chapter on Baeteriology precedes the surgical matter proper, as the author believes, and justly so, that without a clear idea of the causes of infection in its various forms the surgeon is but poorly equipped to guard against it. Fractures and Dislocations, on account of their great practical importance, receive a large amount of space and are treated in a

rational manner, while for all but the more common operations on the Eye, Nose, Throat, and Ear, in common with most gynecological procedures, the reader is referred to special works on these subjects. The different operations on the intestines with their many advocates are carefully considered and clearly set forth with their various advantages and disadvantages, and the chapters devoted to these are both interesting and instructive. There are over seven hundred illustrations, many of them good half-tones, but, on the other hand, there are a number of old cuts which are hardly in keeping with a work in every other respect so up to date. The reproductions of x-ray photographs, of which there are a number, are excellent.

G. M. C.

A DICTIONARY OF MEDICAL SCIENCE. Containing a full explanation of the Various Subjects and Terms of Anatomy, Physiology, Medical Chemistry, Pharmacy, Pharmacology, Therapeutics, Medicine, Hygiene, Dietetics, Pathology, Bacteriology, Surgery, Ophthalmology, Otology, Laryngology, Dermatology, Gynecology, Obstetrics, Pediatrics, Medical Jurisprudence, Dentistry, Veterinary Science, etc. By Robley Dunglison, M.D., LL.D. Twenty-third edition, thoroughly revised, with the Pronunciation, Accentuation, and Derivation of the Terms. By Thomas L. Stedman, A.M., M.D. Philadelphia and New York: Lea Brothers & Co., 1903.

THE name of Robley Dunglison stands forth as that of the greatest incdical lexicographer of the English language. For seventy-five years his work has been the standard dictionary used by the Englishspeaking medical world, and now in its twenty-third edition it is a pleasure to realize that it remains fully up to the standard of the most modern requirements. One thing which is particularly noticeable in the work is the great economy of space which its editor has succeeded in accomplishing by the elimination of obsolete terms and all matter which was not of distinct value in subserving the purpose of the dictionary. In the accomplishment of this object nothing has been omitted which could prove of any real service to the searcher after information, and room has been made to accommodate a wonderful line of new subject-matter. Space has also been obtained by cutting out the figured pronunciation, which is so often absolutely unnecessary. A number of most excellent cuts have been introduced. They have evidently been chosen for their real value, and not to catch the eye of a casual peruser of the work. Although the type is small, as is always necessary in a work of this nature, nevertheless it is so clear that it is easy to read. The publishers of this classical work are to be congratulated in having procured the

services of an editor who, having preserved all the traditions which have given the book its pre-eminence, has at the same time brought it most thoroughly up to date.

F. R. P.

THE AMERICAN ILLUSTRATED MEDICAL DICTIONARY. A New and Complete Dictionary of the Terms Used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry, and the Kindred Branches, with their Pronunciation, Derivation, and Definition, Including Much Collateral Information of an Encyclopædic Character. By W. A. NEWMAN DORLAND, A.M., M.D. Third edition, revised and enlarged. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

AMERICAN POCKET MEDICAL DICTIONARY. Edited by W. A. NEWMAN DORLAND, A.M., M.D. Containing the Pronunciation and Definition of all the Principal Terms Used in Medicine and the Kindred Sciences, along with over Sixty Extensive Tables. Fourth edition, revised and enlarged. Philadelphia, New York and London: W. B. Saunders & Co., 1903.

BOTH these dictionaries have gone through a number of editions, and have achieved a most enviable degree of favor from the medical profession. The large one indeed may be considered as an authoritative work of reference of the greatest value to the literature of the medical profession. Its definitions, though concise, are very lucid. The method of indicating the pronunciation of the terms is exceedingly simple. A feature of special value in the work is the excellent tables of muscles, nerves, bacteria, etc., with which it abounds. Although the illustrations are not very numerous, they are all such as possess real value to the reader.

The American Pocket Medical Dictionary will prove of special use to medical stenographers, nurses, and other persons who are required to be familiar with the definition and spelling of medical terms. Within its small bulk it practically comprises all the information of its nature with which, under ordinary eireumstances, it would

be necessary for them to be familiar.

Both of these dictionaries are most excellent in their typography and their arrangement.

J. H. G.

### PROGRESS

OF

# MEDICAL SCIENCE.

#### MEDICINE.

UNDER THE CHARGE OF

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On the Tuberculous Serum Reaction —MARCHETTI and STEFANELLI (Riv. Crit. d. Clin. Med. Firenze, 1903, vol. iv. pp. 657, 673, 689), in the clinic of Professor Grocco, of Florence, have made an interesting study of the value of the tuberculous serum reaction. As is well known, the possible diagnostic importance of this reaction was first suggested in 1898 by Arloing, whose later studies with Courmont have been followed by numerous observations with conflicting results; one party maintaining that the reaction when carried out under rigid rules and interpreted with proper reserve is of material value in the early diagnosis of tuberculosis; the other, among whom is Koch, denying absolutely its value. The Italian authors have studied seventy-three cases of varying characters. They emphasize the necessity of using cultures of carefully determined age and of following minutely, in every detail, the method of Arloing and Courmont. The results of their studies have been as follows:

They believe that the reaction is of no material value unless positive

within the first six hours.

In grave tuberculosis, pulmonary or abdominal, the reaction was positive in 42 per cent. of the cases.

In early cases, mild or improving, the reaction was positive in 88 per

cent.

In eases which were probably tuberculosis, but which clinically could not be positively determined, the reaction was positive in one out of four of the grave eases and in two-thirds of the milder forms of disease.

In three cases of lupus the reaction was negative.

In five cases which were proven by autopsy not to have been tuber-

culosis the reaction was always negative.

In cases in which clinically there was no evidence of tuberculosis and which did not come to autopsy, the reaction was negative nine times out of ten; it was positive in one instance of multiple sclerosis.

In general, the milder the lesion the more positive was the reaction, while in one case where the reaction was primarily positive it disappared to detail the reaction was primarily positive it disappared to detail the reaction was primarily positive.

peared as death approached (tuberculous moningitis).

For six hours the reaction may be positive in clearly non-tuberculous ases.

They conclude that the Arloing-Courmont reaction, "studied accurately in all its most minute particulars and weighed with duc restrictions, is a useful and not to be neglected diagnostic aid, especially in early and mild cases, the very instances in which the percentage of positive results is larger and more striking." But these cases are the very instances in which, from the point of view of prophylaxis and treatment, the early recognition of the process is of especial value. While they believe that there is a relation between the degree of specific agglutinative power in the tuberculous blood serum and the gravity of the infection, yet, in the present state of our knowledge, the results of the test do not justify prognostic conclusion.

Pneumothorax: An Historical, Clinical, and Experimental Study.— EMERSON (Johns Hopkins Hospital Reports, vol. xi. pp. 1-450) has reviewed the literature of pneumothorax from the time of Hippocrates down to the present date. There are 358 very full abstracts of the most important contributions to the subject during this period. Hippocrates interpreted the splashing sound as a sign of empyema and not of pneumothorax, which he did not recognize. The writer emphasizes the fact that "succussion" is not the splashing sound heard, but the act of shaking which produces it, a distinction which clinicians do not sufficiently realize. Our knowledge of pneumothorax is usually stated to date from the thesis of Itard, published in 1803. He reported 5 cases of pulmonary tuberculosis with pneumothorax, but did not recognize the condition during life. Laennee, who published his observations in 1819, in his work on Mediate Auscultation, was the first to recognize the disease intra vitam. Owing to Hippocrates' belief that the succussion splash was a sign of empyema, it had fallen into disfavor and had been practically disregarded up to Laconce's time. The latter was the first to recognize its true significance and to add it to the symptom-complex. Comparatively speaking, little of importance has been added to our knowledge of the disease since the days of Itard and They discussed the clinical symptoms very fully, and it is Itard's classification, with slight modifications, that is now in usc. Since their day the cases of so-called idiopathic pucumothorax, that is, pneumothorax arising within the chest and in which the gas was not air, have been the cause of considerable dispute. In the last twenty years the therapeutics of the disease has been mainly under discussion.

Emerson reports at length the cases of pneumothorax that have occurred in Professor Osler's and Professor Halsted's wards at the Johns Hopkins Hospital. There were 48 in all. The largest number, 22, were due to pulmonary tuberculosis. Of these, 18 were men and 4 women. In 11 the pneumothorax was right sided and in 11 it was

left sided. Statistics in general have shown the disease to be about twice as frequent on the left as on the right side. Of the 22 cases, 19 came to autopsy, and in 16 the perforation was found. It was in the upper lobe in 7, in the lower in 6, and in the middle in 3. The autopsies on cases of tuberculous pncumothorax represented just 4 per cent. of

all the cases of pulmonary tuberculosis that eame to autopsy.

There were 2 cases following bronchieetasis. There had been only 11 cases previously reported in the literature. Rupture of a metastatic abscess in the lung was the cause in 2 cases. One instance followed gangrene of the lung. Rupture of emphysematous blebs was the cause in 2 cases. Next to pulmonary tuberculosis, the largest number followed tapping of the chest for fluid. There were 10 due to this cause. In 1 the air was pumped into the chest; in a second it was allowed to enter through the unguarded needle; and in a third the lung was pricked by a hypodermic needle. The writer speculates as to the cause in the other cases. 5 of these 10 cases died. In 2 cases the pneumothorax resulted from rupture of an empyema into the lung. Traumatism was the cause in 6 cases. It is of interest that there were 14 other cases in Professor Halsted's wards in which the lung was known to have been injured by various forms of traumatism, but in which pneumothorax did not occur. There was 1 case in which the disease was a sequel to a hepatopulmonary ameebic abscess.

The writer discusses very fully the mcchanics, symptoms, physical signs, course, prognosis, diagnosis, and treatment of pneumothorax. Emerson's original investigations in connection with the disease have been chiefly in a study of its mechanics and also in an endeavor to determine whether the pneumothorax be a valvular, open, or closed one from careful analyses of the gas contained in the pleural cavity. To both of these considerations he has made valuable contributions.

In regard to treatment, the concensus of opinion seems to be that the air in the chest may be usually disregarded. In other words, it is not necessary to aspirate it. If any considerable amount of fluid be present it should be aspirated, but with great caution. Too much fluid must not be removed and too great a negative pressure in the aspirator must be avoided, otherwise a closed pneumothorax may be converted into an open one.

The Results of Organotherapy in Addison's Disease.—E. W. Adams (The Practitioner, October, 1903, p. 473) has analyzed 97 eases of this disease reported in the literature and in which adrenal preparations in one form or other were used medicinally, with the object of determining the efficacy of this line of treatment. He classified the eases, with the results as follows: 1. Cases made distinctly worse, 7. 2. Cases deriving no real benefit, 43. 3. Cases showing marked improvement, 31. 4. Cases permanently relieved, 16. There has been a great diversity of preparations of the gland used. The successful results seemed to occur only in those cases where adrenal gland preparations were given solely by mouth. The subcutaneous and intramuscular injection of the adrenal preparation is uscless, as it has been shown that the active principle is oxidized and rendered inert when injected into the tissues. Adams says that epinephrin and adrenalin, the newly discovered active prineiples, do not appear to have been given a trial. He does not state what preparation of the gland given by mouth seems to have proved

most beneficial. From the post-mortem records he concludes that the cases most likely to derive benefit are those in which the tuberculous process is a chronic selerosing one, and where the other organs are

tairly sound.

The writer states, in drawing his conclusions, that there would appear to be a certain class of cases of Addison's disease which derives indubitable benefit from the exhibition of some form of suprarenal substance, although in any given ease it remains up to now impossible to determine its probable response to the treatment. In any given case, selected haphazard, the probability is that disappointment will follow on the institution of organotherapy; but that probability is very distinctly less than that attaching to any alternative method of treatment at present known. He believes that the last word upon the preparation to be used and its method of administration remains to be said. The problem seems to be to get a sufficient and continuous dose of the pure and active principle unchanged into the blood stream. Intravenous injection is held to be impracticable.

#### SURGERY.

#### UNDER THE CHARGE OF

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#### AND

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The Treatment of the Appendix Stump after Extirpation.—Rieder (Centralblatt j. Chir., 1903, No. 51) states that he differs most widely from the remarks of Zellar (an abstract appears in this number), and that the best method is as follows: the mesentery should be freely separated from the appendix and then the appendix should be ligated with catgut close to the gut. Catgut is preferable to silk, as it can be tied tighter, and it does not tend to injure the bowel. The appendix should again be ligated, this time with silk, 1 cm. away from the first ligature and then divided between them. The mucous membrane of this stump should then be excised with seissors and the remaining coats should then be closely approximated with three silk interrupted sutures; the temporary eatgut ligature which was first applied should then be cut. In asceptic cases no drainage is necessary, but if indicated one should not he sitate to use it.

Extirpation of the Appendix.—Zeller (Centralblatt f. Chir., 1903, No. 45) states that one method of treatment of the stump of the appendix after extirpation is to leave a "cuff," which is then sewed over the stump; still another consists in the turning in or invagination of the stump into the excum, and then the area is closed by Lembert sutures. This method, however, may produce dangerous sequelæ, such

as abscess, as in the case reported by Herman (Centralblatt f. Chir., 1901, p. 1028), where the patient succumbed five days after operation from this cause. The author recommends as the best procedure to separate the appendix from its mesentery and then, taking care to prevent the escape of any of the intestinal contents, to cut it absolutely flush with the bowel, and then to close the resulting hole in the gut by two rows of Lembert sutures. This method has uniformly been followed by a good result and would seem to be the safest method of avoiding the formation of a fecal fistula.

The Treatment of Granulating Wounds.—WAGNER (Centralblatt f. Chir., No. 50, 1903), after discussing in detail the treatment of these wounds by means of different ointments and aseptic dressings, states that his efforts have been directed toward lessening the period of granulation. In the large superficial wounds skin grafting has proved most cfficacious on many occasions, but it is a useless procedure in the presence of active suppuration. In those cases where the granulations have a tendency to be ædematous and as a result the dressings are kept constantly moist by the discharge, ointments will prove to be useless, as they only tend to increase heat and moisture and at the same time absolutely prevent the contact of the air with the wound. If such cases have their wounds exposed to the air during the daytime one will soon see the whole aspect change; the secretion becomes much less and healing follows. At night they should be covered by a suitable dressing to prevent infection from the bed-clothes. The author notes having selected two practically similar cases and treated one by the "open" and the other by the "closed" method, and the one treated by the former method healed in much the shorter space of time. In no case did any infection result from the exposure of the wounds to the air.

A New Operation for Hemorrhoids.—Landström (Centralblatt f. Chir., 1903, No. 47) states that extirpation and cauterization are well-known methods and that the treatment by ligature has also many advocates, but that lately he has used the following method in his hospital work, with excellent results. The principle of the operation is to exert strong pressure by means of forceps on the hemorrhoidal mass, which is thus excised. The blade of these forceps is about 7 cm. long by 5 cm. wide; they should be applied in a similar manner to the Langenbeek forceps. The patient is prepared in the usual manner, then placed in the side position, the sphincter dilated, the forceps applied, the hemorrhoidal mass removed, and the operation completed by the introduction of some iodoform gauze, which, however, should be removed on the second day. The operation requires but very few moments for its performance and the hæmostasis is nearly absolute, and so the operation is an admirable one for weak patients. The author notes the successful use of this method in 25 cases, and has found it to be a most satisfactory method of procedure.

The Radical Cure of Inguinal Hernia, with Especial Reference to the Anatomy.—Horman (Centralblatt j. Chir., 1903, No. 41) bases his observations upon an experience of 45 cases during the past year upon whom the radical cure was attempted. The most perfect asepsis is an absolute essential, for upon it depends the success of the operation.

Too much importance cannot be laid upon the absolute closure of the sac in the region of the parietal peritoneum and the restoration or re-establishment of a support for the same at the internal ring by one or more wire-thread sutures, but care should be taken at this time not to disturb the normal relation of the spermatic cord. This presents no extraordinary difficulty if proper care be taken in the insertion of a purse-string suture into the sac and in the subsequent sutures. The author's series of 45 cases made an uninterrupted recovery, and when examined a year later showed no evidence of reenrence.

#### THERAPEUTICS.

UNDER THE CHARGE OF

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Treatment of Mucomembranous Enterocolitis .- Dr. Perochaud asserts that the three principal indications in this affection are these; to modify the general state of the nervous system, to modify the local nervous condition, and to excite the trophic action of the abdominal nerves. If the disease is of long standing absolute quiet and milk diet must be enjoined. In the eases of short duration, in addition to milk, cereals, soft-boiled eggs, small quantities of the various ments-ent very fine-fish and the green vegetables are allowable. Fruit, if eaten at all, must be cooked, and bread should be eaten in small quantity. No fat some may be taken. Water is the preferable beverage, but beer and wine together with the mildly alkaline mineral waters may be drunk in small amounts. Beverages are useful to combat the tendency to constipation, and milk drunk during meals often renders service in this connection. Highly sensoned food should be interdicted. In severe forms of the disease where absolute milk diet is intolerable, cereals and finely chopped meat may be given. It is very necessary that a daily movement of the bowels should be seeured, but this must be done without irritating the intestine. The author recommends for this purpose injections of olive oil and easter oil by the mouth, but other laxatives may be employed; most important is the acquirement of the habit of going to stool every day at the same hour. Abdominal pain may be relieved by hot applications, cannabis indica, belladonna, and, as a last resort, morphine. Abdominal massage is useful in this connection as well as in combating the constipation. Intestinal lavage is to be employed for the removal of the products of the disease from the intestine. It should be given through a tube passed high into the reetum, and in atonic conditions of the intestine should be at a temperature of 103° F., while, if the opposite state obtains, at 98° F.; the quantity should be about two quarts and the procedure should take at least twenty minutes. Various solutions may be used. Naphthol, 1:300; ichthyol, 1:64; or solutions of sodium bicarbonate, sodium ehloride, sodium borate, silver nitrate, etc. The author highly recommends beer yeast to be taken in closes of about one-half a drachin

slightly diluted three times a day between meals, and asserts that his results from its use have been most excellent. General tonic treatment should also be prescribed, but the greatest care should be observed lest the digestive tract be disturbed by it. Massage, hydrotherapy, and electrotherapy, especially the latter, are important adjuncts to the other treatment. Gazette médicale de Nantes, 1903, No. 51, p. 1021.

Wine and Alcoholic Beverages in Dyspepsia.—Dr. Albert Mathieu considers that the routine use of alcohol in gastric disorders is not to be tolerated, though Boas has shown that in small quantities it stimulates stomach digestion. Alcohol, when injected directly into the organ, has a direct action upon its lining and a chemical action upon its contents. Linossier has shown that alcohol diminishes the peptonizing power of the gastric juice and has the same action upon the trypsin. Alcohol also retards the inversion of saceharose in the presence of beer yeast. Dastre has proven as well that it also interferes with pancreatic digestion. It is therefore evident that in marked gastrie lesions, such as uleer, cancer, gastritis, with eongestion of the peptie glands or atrophy of the same, alcohol is contra-indicated not only because it retards digestion and increases the pain, but also since it aggravates the lesion. The patients who appear to be benefited by the use of alcohol are those whose stomachs lack motor power and who have a sensation of weight or inflation after eating. Such find relief from a small glass of eognae or liqueur at the end of a meal. It is probable, however, that even in these eases the habit increases their disease in the end. They may better take a glass of hot, well diluted, red or white wine during or after the meal from time to time. The author believes that patients troubled by acid regurgitation may be relieved by taking white wine, preferably sparkling, well diluted. Wine, especially red wine, increases the discomfort of those with a tendency to gastrie stasis and distress. In all eases the use of wine should be left off and renewed from time to time if it is to produce its best effect.-Revue de thérapeutique, 1903, No. 23, p. 798.

Renal Opotherapy.—M. RENAULT has administered the macerated kidney of the pig in various forms of renal disease with striking results. He states that this form of medication rapidly induces diuresis, and when continued brings the quantity of urinary secretion to normal and maintains it. It reduces the quantity of albumin excreted by the insufficient kidney and often causes its entire disappearance for considerable periods, consequently it favors the restoration of the epithelium of the organ to a histologically normal condition. The macerated kidney also exercises an antitoxic action and the antitoxin which it contains is not changed by the digestive processes. In some patients. mild toxic symptoms may be produced, such as pruritis, urticaria, sudorific crises, slight gastric disturbance, etc., but aside from these its action is entirely beneficial. Arterial hypertension, excitability of the heart, and tendency to dilatation always lessen under its influence if it is administered for a sufficiently long time. It is a therapeutic agent that should be in general use, not as a substitute for other medication, but as an adjunct to it. The chief disadvantage of the treatment is that the kidney must be prepared freshly every day. - Gazette médicale de Paris, 1903, No. 52, p. 454.

The Prophylaxis of Gonorrhea.—Dr. Jules Janet, after considering the use of most of the means recommended for the prevention of gonorrheal infection, such as the condom, the application of vaseline to the meatus before coitus, and the injection of various antiscptics (mercury bichloride 1:1000 to 1:10,000; silver nitrate, 2 per cent.; protargol, 4 to 20 per cent.), concludes with the statement that, while he recommends to his patients the instillation into the fossa navicularis of several drops of a solution of silver nitrate 2 per cent., or of protargol 20 per cent., he believes the only true prophylaxis of the disease is not to lay one's self liable to infection.—Revue de thérapeutique, 1903, No. 24, p. 829.

The Internal Treatment of Gonorrhea.—DR. EDMUND SAALFELD reports excellent results in a considerable number of cases from the internal administration of capsules of gonosan, which is a preparation of the resin of kava-kava and sandal oil. Under this agent the purulent discharge in a short time becomes mucoid, the pain is diminished, painful erections are rendered less frequent and distressing, and complications, such as epididymitis, prostatitis, cystitis, and adenitis are unlikely to occur. The author believes that gonosan is of especial value in patients in whom local treatment for any reason cannot be frequently applied.—Therapeutische Monatshefte, 1903, No. 12, p. 626.

Extract of Thymus in Chloroanæmia.—Dr. G. MARCOLONGO has experimented with the extract of the thymus gland in the chloroses of childhood and adolescence and has found that in five patients, varying in age from eight to twenty-one years, the hæmoglobin percentage and the number and resistance of the red cells rapidly increased. At the same time a considerable amelioration of the general condition and an increase in weight was noted. The preparation employed contained one part of the juice of the gland suspended in two parts of neutral glycerin. Of this, two and one-half drachms were given each morning and night.—La semaine médicale, 1903, No. 50, p. 412.

Potassium Iodide in Ophthalmology.—Dr. A. Leprince has had occasion to use this drug in various ophthalmic lesions, infantile cataract, episeleritis, seleritis, and iridocyclitis. In all the cases considerable improvement was shown after the first day and cure followed after varying periods of time, depending upon the severity of the disease. In rheumatic and arthritic lesions the treatment is especially applicable. The iodide is employed in strengths of from 1 to 2.5 per cent., depending upon the nature of the affection. Of this solution, from two to three drops are instilled into the eye from one to three times a day. The procedure is painless and provokes no reaction. In the author's opinion severe cases might be benefited by subconjunctival injections of the solution.—Revue française de médecine et de chirurgie, 1903, No. 57, p. 1361.

Sodium Salicylate in Lupus.—Dr. A. Plaque calls attention to the use of sodium salicylate in two cases of lupus under his observation. Villemin the younger has experimented upon cultures of the bacillus tuberculosis and has found that only six agents produced complete sterilization; of these, four were salicylic acid derivatives, of which

sodium salicylate seemed most applicable to the purpose in hand. The drug was used in the following solution: sodium salicylate, 1; distilled water, 8. Applications of this were made morning and evening to the involved areas. The only untoward effect produced was a slightly disfiguring white pelliele. The addition to the solution of a little fuchsin produced a rose color and greatly lessened the disfigurement. This latter should be added in as small quantity as possible, so as not to diminish the tolerance of the tissues and not to increase the irritation. The two cases treated were of long standing and obstinate facial lupus; in one six weeks and in the other one month of treatment produced a considerable amelioration. The cures are not complete, since certain small hard nodules remain. The author suggests that it would be interesting to inject the solution into these, but before doing this it would be well to further observe the results of topical application.—

Journal de médecine et chirurgie pratique, 1903, No. 24, p. 929.

#### OBSTETRICS.

#### UNDER THE CHARGE OF

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Distention of the Lower Uterine Segment Before the Rupture of the Membranes.—Goldner (Monatsschrift für Geburtshülfe und Gynäkologie, Band xviii., Heft 4, 1903) contributes an interesting and prae-

tically important paper upon this subject.

He ealls attention to reported cases of rupture of the uterus in which the ovum has been expelled into the abdominal eavity with unruptured membranes. His own observations eover a period of about three years with 9000 eases of labor, among whom there were 321 eases in which the lower uterine segment became abnormally distended, and of these in 19 this distention occurred before the rupture of the membranes. From these cases he concludes that this distention arises from the great predominance of the muscular tissues in the contractile segment of the uterus. He finds that a long continuance of labor pains, repeated labor, and early rupture of the membranes all tend to produce this condition. In his 19 cases, 17 were primiparæ of the average age of childbearing. No disease which might affect the muscular tissue of the uterus was present in these eases. The children were not abnormally large, nor were there pelvic conditions which obstructed birth. In 7 of the 17 eases the eranium remained high and movable above the entrance to the pelvis. Oligohydramnios was present in 9 of the 19 cases, five times with normal pelvis and four times with contracted pelvis. Some pelvie contraction was present in 8 cases, although but 3 of these had contraction sufficiently great to influence the course of labor. In 6 eases there was absolutely no abnormality to which could be ascribed the coudition. Toughness and resistance of the membranes with oligohydramnios and a rigid and undilatable external os were the conditions which seemed to predispose to abnormal distention of the lower uterine segment with mirroptured membranes. In 15 of these eases the contraction ring was as high as the numbrication. In 10 cases the contraction could be plainly discerned immediately

In 13 of these patients it was necessary to interfere to expedite labor. It was in all these cases possible to examine the patient before active pains came on and to be sure that the membranes had not ruptured after the birth of the child. through a laceration in the membranes high above the presenting part.

Tubal Gestation in Which the Ovum Continued to Grow about Four Weeks after Rupture, Becoming Implanted on the Omentum. -Lockyer (Journal of Obstetrics and Gynecology of the British Empire, November, 1903) publishes the case of a patient who had attacks of irregular abdominal nain accommanied by collabora. irregular abdominal pain accompanied by collapse. A critical examiration of the history revealed the fact that the nation had bed four rregular abdominal pain accompanied by conapse. A crucial examination of the history revealed the fact that the patient had had four liation of the history revealed the fact that the patient had had four liation of the history revealed the fact that the patient allowed the shadomen distinct attacks of internal homographs. distinct attacks of internal hemorrhage. The left side of the abdomen was tender and considerably swollen, and upon opening the abdoment the opening the abdoment the opening the openin the omentum was pushed upward by extravasated blood. The fetus appeared in the wound and the placents had been attached to the the omentum was pushed upward by extravasated blood. The rectise appeared in the wound and the placenta had been attached to the omentum near the left broad ligament. The placenta had also been of the policy brim of the rectum and the side of the policy brim attached to part of the rectum and the side of the policy brim attached to part of the rectum and the side of the policy. omenium near the left broad algament. The placenta had also been The attached to part of the rectum and the side of the pelvic brim. The attached to part of the rectum and the packing and stimulation was general coving was stopped by gauge packing and stimulation was general oozing was stopped by gauze packing and stimulation after treely employed. The nation died in collabor twenty-four hours after general overing was stopped by gauze packing and sumulation was freely employed. The patient died in collapse twenty-four hours after operation Upon examination the fetus was four months advanced. There Upon examination the fetus was four months advanced. There was no attempt at the formation of an hamatocele, but the pregner had been secondary abdominal pregnence the tube having runwas no attempt at the formation of an mematocere, but the preg-nancy had been secondary abdominal pregnancy, the tube having rup-tured in the corby weeks of gostation followed by the temporary recovery nancy mad been secondary abdominal pregnancy, the tube having ruptured in the early weeks of gestation followed by the temporary recovery tured in the early weeks of gestation followed by the tube, had gained of the mother. The villi, penetrating the wall of the neritoneous and to the neritoneous attachments upon the omentum to the rectum and to the neritoneous attachments upon the omentum. operation. or the mother. The vini, penetrating the wan or the mother, may gamed attachments upon the omentum, to the rectum, and to the peritonenn of the broad ligament. The fetue remained

forming the posterior layer of the broad ligament. The fetus remained alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and alive until it passed through a large tear in the secondary gostation and the secondary gostat forming the posterior myer or the oroad figuration. The remained alive until it passed through a large tear in the secondary gestation sactions alive until it passed through a large tear in the secondary gestation sactions. A Statistical Study of Eclampsia.—In the Archiv jür Gynükologic,

RETURN CONTRIBUTES the results of an extension Band Ixx., Heft 2, 1903, BUTTNER contributes the results of an extensive estatistical study in columnsia. Dana IXX., Melt Z, 1908, BUTTNER contributes the results of an extensive statistical study in columpsia.

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The results of the fact that in districts where physicians could be ment are shown in the fact that in districts where physicians could be contrast with a previous mortanty of 5±.5 per cent. The results of treatment are shown in the fact that in districts where physicians could be ment are shown in the fact that in districts where physicians could be ment are shown in the fact that in districts where to 97 4 per cent. In three obtained with difficulty the mortality rose to 97 4 per cent. obtained with difficulty the mortality rose and the patients perished cases diagnosis was not made during life and the patients. obtained with dimenty the mortality of columns of columns of during life and the patients perished undelivered. The mortality of columns of columns of during labor was undelivered. cases anguosis was not made during and the patients personed auring and the patients personed auring labor was undelivered. The mortality of celampsia occurring during labor was undelivered. 20.5 per cent. Where eclampsia developed after labor the mortality was 24.07 per cent. The longer after delivery the eclampsia occurred, the better the prognosis for the mother. If, however, eclampsia develops during the latter portion of the first day after labor, the mortality rises

eonsiderably.

The mortality for the fetus was 29.7 per ecnt. Here again among cases in the country and in small hamlets the mortality among children was greatly increased, rising to 32.4 per eent. About 50 per cent. of the mothers required artificial delivery. It is shown that prompt interference during labor, resulting in the rapid delivery of the child, improves the mother's chances in those eases where eclampsia develops during parturition. When the mother dies of eclampsia during labor, fetal mortality is enormously increased. In cases where the mother dies after the delivery of the child the chances of the fetus for survival seemed to be fairly good.

Regarding the repetition of eclampsia in the same patient, it was found that 2.40 per cent. of the patients had eclampsia more than once. The effort was made to determine the influence of the weather upon the occurrence of eclampsia, and it was found that the colder months showed an increase in the percentage of cases. The percentage of moisture in the atmosphere seemed to influence the occurrence of eclampsia, as the drier the air the better the conditions for the patient. Extremes of heat or cold were both marked by an increase in eclampsia.

Regarding the question as to the relationship existing between cclampsia and labor pains or contractions of the uterus, it was determined that cclampsia is not eaused by labor pains, but that eclampsia first occurs and then uterine contractions. Both contractions of the uterus and eclamptic convulsions result from irritation of the same poison

poison.

As regards the occurrence of eclampsia in epileptic women, upon elose examination of the history of eases, but two could be found in which it seemed probable that epilepsy and eclampsia occurred in the same person.

### GYNECOLOGY.

UNDER THE CHARGE OF

HENRY C. COE, M.D.,

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

Epithelial Spaces in Lymph Nodes—Falkner (Zentralblatt für Gynäkologie, No. 50, 1903) found in 13 per eent. of Wertheim's eases of radical operation for cancer of the uterus peculiar spaces within the lymph glands lined with columnar epithelium. Eighty cadavers were examined (not cases of cancer) and the pelvic glands were studied microscopically without showing any of these spaces. Hence the inference that they are not related to the Wolffian bodies (as thought by various observers), but to the uterine carcinoma. Observations by

Meyer have subsequently shown that these may be due to some other irritation. The inference that these spaces always represent beginning cancerous degeneration is not correct, though in some instances Wertheim demonstrated the presence of epitheliomatous invasion of the spaces.

Exfoliative Endometritis.—Gottschalk (Zentralblatt für Gynäkologie, No. 49, 1903) describes a specimen in which it was shown that the exfoliation was due to hemorrhage into the submucous layer. Numerous yenous thrombi were present, indicating obstruction and resulting rupture of the vessels, doubtless due to diminished cardiac action. This was also indicated by the presence of slight ædema of the lower limbs. Although repeated curettement and intrauterine applications had failed to relieve the membranous dysmenorrhæa, it was cured by remedies indicated by the cardiac weakness.

Drainage.—Martin (Chrobak's Festschrift; Zentralblatt für Gynä-kologie, No. 49, 1903) believes that it is impossible to predict before operation in a given case whether pus is infectious or not, although examinations of the blood are undoubtedly of value. It has been the writer's practise not to drain after laparotomy unless marked leukocytosis is present, and especially if a pus-sac is removed without rupture. If the intestine is injured or there are large raw surfaces which cannot be covered with peritoneum, the gauze tamponade is used and the ends are carried through both the abdominal and vaginal openings.

Modern Gynecological Operations.—Fritsch (Ibid.) criticises the tendency of surgeons to adopt routine methods of procedure. While the vaginal route is preferable when a tumor is readily accessible, he believes that in the majority of cases abdominal section will be attended with the best results, whether the case is one of uterine fibroid, adnexal disease, or extrauterine pregnancy. He thinks that, while Alexander's operation is safer, ventrofixation gives the best results, and both are superior to vaginofixation.

Preservation of the Ovaries after Total Extirpation of the Uterus.

—Leopold and Ehrenfreund (Ibid.) reports the results in 151 cases of vaginal hysterectomy for fibroids. The operation was limited to the removal of tumors not larger than a child's head. Ligatures were used, the mortality being only 3.9 per cent. Or of 102 patients who were kept under observation, all but four made were able to attend to their usual occupations. Although one or both ovaries was preserved, climacteric disturbances were frequently noted, though never so severe as to affect the patient's general health.

Fibromyoma of the Vagina.—Potel (Revue de Gynécologie, Band vii., Heft 2-4) adds 2 cases to 160 in the literature. Eighty-four per cent. occurred in young women. The pedunculated form is most common, and 50 per cent. occur in the anterior vaginal wall. They grow slowly their growth being accelerated by pregnancy. In all but 6 cases the neoplasm was a fibromyoma. The only treatment is extirpation, which may require careful dissection from the rectum and bladder and ligation of the nutrient vessels, especially in the case of sessile growths.

Leukocytosis in Inflammatory Disease of the Adnexa.—Kirchmayr (Wiener klin. Rundschau, No. 11, 1903) found marked leukocytosis in all his cases of parametrie and perimetric abscesses, 17,190 being the highest count noted. In several instances in which no pus was found the number of leukocytes was doubled after operation, probably due to fresh lymphatic infection. The writer infers that a leukocytosis of 30,000 points with great probability to the presence of pus, but that a moderate increase in the number of white cells is of little diagnostic value. The fact that there is no increase is not evidence that pus is absent.

Drainage in Laparotomy —Doderlein (Zentralblatt für Gynäkologie, 1903, No. 471) drained the pelvie eavity per vaginam in 161 out of 754 abdominal sections (21.3 per cent.), with a mortality of 8.7 per cent., losing only 2.3 per cent. of the patients where no drainage was employed,

though in the former series the eases were more serious.

Fehling (Ibid.) prefers drainage through the abdominal wound with a Mikuliez tampon. He drained only thirty-six times in 327 laparotomies, his general death rate being 4.5 per cent. In 55 pus cases (with a mortality of 1.8 per cent.) the Mikulicz tampon was used in 28, with 1 death; in 27 cases without drainage there was no mortality.

#### OPHTHALMOLOGY.

UNDER THE CHARGE OF

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AND

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Possibility of Radium Rays in Blindness.—Tracy (Journal of Advanced Therapeutics, December, 1903) refers to the use of radium in optic atrophy and reports a case. Giesel's observation that when a tube of radium touched the cyclids of the closed eyes a sensation of light was produced, has suggested the attempt to employ this property to stimulate the optic nerve in cases of blindness from nerve disease with retention of light perception. Lunden, of Berlin, affirms that he obtained good results from radium in the case of two boys who were almost totally blind.

Tracy reports improvement in the case of a man fifty-two years of

age who had been affected with optic atrophy for four years.

Cataract Extraction, with a Small Peripheral Buttonhole in the Iris; Report of 312 Cases.—Chandler (Archives of Ophthalmology, January, 1904) removes a piece of iris 1 mm. in diameter as near to its root as possible to prevent prolapse; the opening permits drainage of the aqueous and expression of the cortex. He usually makes it

after extraction of the lens. It is necessary to use a forceps the teeth of which are at the tip end, and seissors with very thin blades.

Three hundred and twelve senile entaracts operated on by this method with one or two exceptions gave the following satisfactory results: vision above  $\frac{1}{10}$ , 91.2 per cent.;  $\frac{1}{20}$ , 3.5 per cent.;  $\frac{1}{30}$ , 2.6 per cent.; fingers and projection, 1.2 per cent.; lost 1.5 per cent. There were 4 cases of prolapsed iris, 2 the direct result of accidental violence after re-establishment of the anterior chamber. Iritis occurred in varying degrees in 32 eyes, with blocked pupil in 3 cases; 4 eyes were lost, 3 from corneal suppuration and 1 from panophthalmitis. Secondary operation was performed in 67 cases without any inflammatory reaction.

The average stay in the hospital was eighteen and two-third days.

Sympathetic Ophthalmia.—RAMSAY (Annals of Ophthalmology, January, 1904) details the morbid changes in the exciting eye which are likely to give rise to sympathetic inflammation, such as penetrating wounds of the eiliary region, foreign bodies lodged within the eyeball, degenerative changes in an eye previously injured, corneal ulcers which have perforated. Sarcoma of the choroid or dislocation of the lens aecompanied by plastie iridocyclitis may also induce sympathetic inflammation; but these are probably the only instances in which the disease arises apart from a perforating lesion of the exciter. disease probably never occurs earlier than three weeks; after that there is no limit. On an average it develops most frequently five or six weeks after the accident. If the second eye escape until the one injured has healed, it will probably not occur at all unless fresh inflammation or degenerative changes occur in the exciting cyc. It is more frequent in the young than in the old. Its onset is most insidious. Scrious results are frequently not anticipated until the disease is thoroughly estab-The prognosis is always grave.

Sympathetic inflammation must be distinguished from irritation; the latter is simply a neurosis and passes off without leaving any organic

changes.

Mackenzie was the first to demonstrate the causal connection between the exciter and the sympathizing eye. He considered that the disease was transmitted by the optic nerve across the chiasm. Leber and Deutschmann have advanced the theory that sympathetic inflammation was the result of a septic infections process in the injured eye and that the micro-organisms travelled along the optic nerves to the sound eye. Unfortunately subsequent investigations have failed to verify these eonclusions and they are now generally discredited. All clinical experiences, however, go to support the theory that infection of the injured eye is necessary to cause inflammation in the other, but there seems no reason for supposing that a specific micro-organism is necessary. Injury of one eye is itself capable of producing nutritional disturbances in the other, but in addition to such vasomotor changes another factor must be present before true inflammation is excited; this other factor is no doubt microbic infection. The difficulty lies in demonstrating the channels of communication between the two eyes along which the microbiotic factor finds its way. There are three such passages: the bloodvessels, the ciliary nerves, and the optic nerves. The latter can be excluded from the clinical phenomena. It would appear that the infecting influence, microbe or toxin, reaches the sound eye through

the blood stream and that its virulence is concentrated upon the anterior uveal tract, whose nutrition has already been lowered by the irritation

of the ciliary nerves of the injured eye.

Enucleation of a severely injured eye is advised except under two circumstances, first, when there is still sight in the injured eye and no sign of sympathetic disturbance in its fellow; and, second, when sympathetic inflammation is in progress and there is still sight in the exciting eye.

The usual antiphlogistic regimen and treatment for iridocyclitis are

recommended, special stress being laid upon mereury.

No operation ought to be attempted until some time after all acute symptoms have subsided.

#### DERMATOLOGY.

#### UNDER THE CHARGE OF

LOUIS A. DUHRING, M.D.,

PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA,

#### AND

#### MILTON B. HARTZELL, M.D.,

INSTRUCTOR IN DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

Erythrodermia Exfoliativa Universalis Tuberculosa.—BRUUSGAARD, (Archiv jür Dermatologic und Syphilis, Bd. lxvii., Heft 2), as a contribution to the study of tuberculous affections of the skin, reports the ease of a woman, sixty-three years old, who developed an inflammation of the skin which, at first limited to the calves, in the course of some months became universal. The inflammation was accompanied by marked redness, infiltration, and exfoliation, without moisture. Upon the entrance of the patient into the hospital there was marked swelling of all the palpable lymph glands. The hair and nails were implicated early in the disease, and were gradually east off. The severity of the inflammation increased, and a marked tendency to acute exacerbations appeared with increased exfoliation. The exacerbations were often accompanied by increased fever, dyspnæa, and intolerable itching. the patient's general condition grew worse the exacerbations diminished in intensity and frequency. The final stages of the disease were characterized by increasing cachexia, a peculiar pigmentation associated with the follicles, and universal swelling of the lymph glands. The patient finally died of bronchopneumonia. At the autopsy the lymph glands were found to be markedly swollen and to contain large and small broken-down foci in which numerous tubercle bacilli were demonstrable. The liver and splcen also contained isolated miliary tubercles with giant cells, and the ilcum contained a tuberculous ulecr. Sections of skin taken from various parts of the body showed typical tubercles with giant cells and bacilli. The tubercles were situated in the papillary and subpapillary layers of the skin, and in a single section were found plainly localized about a hair follicle.

A Year's Trial of the Light Treatment for Lupus.—C. M.O'Brien (Dublin Journal of Medical Science, August, 1903) used the French Lorbet-Genoud lamp, usually fifteen minutes being allowed for each sitting, and the current 12 ampères, but where it was tolerated by the patient, longer sittings were made use of (twenty to sixty minutes), with from 12 to 18 ampères. The author thinks that some of the failures attributed to the French lamp compared with the results from the Danish lamp. Lengthening may be overcome by the sittings. In cases attended with ulceration, where the pressure of the Danish method could not be tolerated, the Roentgen rays were used until sufficient healing had occurred to permit of further treatment by the ultra-violet rays. The results of the anthor upon the whole were highly satisfactory, and he thinks, as to permanency of cure, that the Danish light cannot be excelled. In circumscribed superficial lupus the Danish (Finsen) light, properly used, takes a conspicuous position among the most notable discoveries in modern medicine.

A Case of Erythema Induratum (Bazin) Combined with Lichen Scrofulosorum.—Julius Sollner (Monatshefte für prakt. Derm., December 15, 1903) gives full notes of the ease, with microscopic examination of the lesions. No tubercle bacilli were found. After consideration of the various relations of the two diseases, he concludes that the manifestation of erythema induratum is either tuberculosis or is related to that disease in a manner like that of lichen serofulosorum to tuberculosis.

Protozoa in a Case of Tropical Ulcer ("Aleppo Boil").—J. II. WRIGHT (Journal of Cutaneous Diseases, January, 1904) states that this disease, which is generally believed to be of an infections nature and capable of transmission from one individual to another by inoculation, but apparently not contagious in the usual meaning of that term, has considerable resemblance to tuberenlosis and syphilis of the skin. A case was observed in Boston in the person of an Armenian child, aged nine years. In thin stained smears peculiar bodies having the following characters were discovered. They were round, sharply defined, and 2 to 4 micromillimetres in diameter. In each of the bodies there was a larger and a smaller lilae-colored mass. These bodies were present in very large numbers in the smears, and there is good reason for believing them to be micro-organisms and the infections cause of the disease, and further that they are protozoa. Reference is made to the studies of other observers in the same disease. Photographs accompany the article.

Pyæmic Dermatitis.—Leber (Annales de Dermatologie et de Syphiligraphie, No. 12, 1903), after a brief résumé of the literature concerning some of the dermatoses which occur as a complication of or, in some instances, as the chief symptom in general infections diseases, reports a case of emption consisting of pustules, macules, deep-scated nodules, and abscesses in a boy, aged seven years, as a sequel of an infected wound of the heel. The anthor's conclusions concerning pyæmic inflammations of the skin are as follows: In pyosepticæmic infections there are dermatoses produced by microbes (staphylococci and streptococci) brought to the skin through the bloodyessels—metastatic

pyæmic dermatoses. These dermatoses may be multiform (purpuric, pustular, varioliform, and nodosc). There is no reason for placing these affections in the group of angioneuroses; they are not crythemata, but inflammations. Bacteria may form superficial metastases in the capillaries of the papillæ, in the derma, or in the subcutaneous connective tissue, in the last case affecting the veins by preference. The virulence of the microbes brought to the skin by the blood seems to be at times attenuated by this transportation, as suppuration may be absent even in the presence of pyogenic micro-organisms.

A Rare Form of Xanthoma.—W. Moser (New York Medical Journal, October 10, 1903) records the case of an Italian boy with multiple, mushroom-like growths, varying in size from a pea to a hen's egg, of a bright yellow or yellowish-pink color, neither sensitive to pressure nor painful, smooth and not nodulated, tuberculated, nor fissured. They had existed for a long period and gave rise to no symptoms beyond the discomfort of their presence. The microscope showed them to be made up of a yellow fibrous tissue, the eellular elements being seanty, polymorphic, and pigmented.

#### HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

CHARLES HARRINGTON, M.D.,

Malaria in Places Usually Free from Anopheles.—Several cases are communicated by Dr. John Cropper (Journal of Hygiene, October, 1903, p. 515) illustrative of a difficulty which often occurs to those who study the agency of anopheles in the causation of malaria and which has lcd sometimes to disbelief in such agency. In a former paper on the "Geographical Distribution of Malaria in Upper Palcstine" (Ibid., 1902, p. 47) he had said that, although resident for some years in the town of Aerc, he had never been able to find a single specimen of anopheles. This year his successor had two patients ill with malaria, and in their room the anopheles were found. The disease is rare in Aere, but common chough a mile away. The preceding winter was exceptionally wet, and the water covered the plain to within less than a half-mile from the town, near the wall of which the house of the patients was situate. At Shefa Amr, three hours from Acre, within reach of no running water except after heavy rains, two English ladies had malaria. Imagines of anopheles were not found, but the water of an open cistern contained the larvæ. At Nahlous, where, in 1901, anopheles larvæ were found in a shallow eistern, an examination of several open eisterns in houses where the disease occurred gave negative results. Visitors come often from notoriously malarial districts within easy reach and introduce the parasite. "So it is, probably, with many if not all places in the Tropics not essentially malarious—i. c., not furnished with an abundant supply of anophcles."

Formaldehyde Disinfection.—In disinfection of rooms with formaldehyde, the gas tends toward the eeiling, in spite of the fact that its specific gravity is slightly greater than that of air, and so the upper parts are more thoroughly disinfected than the lower. To overcome this irregularity, Mayer and Wolpert (Archiv für Hygiene, vol. xliii. p. 171) introduced a rotary fan, which brought about a better result. The influence of temperature is shown by the fact that at temperatures below freezing the gas has no influence whatever on anthrax spores. Each degree increase beyond 50° F. to 60° F. shows a distinct increase in efficiency, and at 86° F. the action is very marked. (Ibid., p. 222.)

Toxicity of Coal-tar Colors.—In Russia the use of coal-tar colors in articles of food and drink was prohibited in January, 1898, but nevertheless they are largely employed. For example, fourteen of fifteen confections examined at Dorpat were found to be so colored, and about the same results have been obtained at the public laboratories at Moscow, St. Petersburg, Odessa, Kiew, and Warsaw. In order to determine their toxicity, Professor G. W. Clopin (Hygienische Rundschau, August 1, 1903) examined 50 colors, which he gave to dogs in 1-gram to 3-gram doses daily for eight to fourteen days, and also applied to human skin, the subjects wearing woolen or cotton gloves or stockings which had been dved with the various colors without the use of poisonous mordants. Of the 50 examined, 15, or 30 per eent., proved to be decidedly poisonous, either causing death of the dogs or such severe symptoms of poisoning that they would have died had the experiments continued, and 20, or 40 per cent., were found to cause disturbances of limited extent. Of the distinctly poisonous colors, only 2, ursol D and auramin O, proved to be skin poisons. Ursol D eaused severe dermatitis and auramin O irritated the skin only feebly. Like other investigators, he found no red color to be poisonous.

## PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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A Note on Autolysis in Lobar and Unresolved Pneumonia.—FLEXNER (Univ. of Penna. Med. Bull., 1903, vol. xvi. p. 185) concludes from a long series of experiments made with specimens of typical lobar pneumonia in various stages of the disease, and with ten or twelve examples of unresolved pneumonia, that the process of resolution is in main part accomplished by the self-digestion of the exudate in the pneumonic

lung. When protected from the action of bacteria lungs in the stage of grey hepatization were found to undergo autolysis outside the body with great rapidity, while the specimens of red hepatization took much longer to autolyze and those of unresolved pneumonia showed scarcely any change, even after a considerable length of time. The process of autolysis is mainly dependent upon the number of leukocytes in the exudate, and it is this fact which explains the slow and incomplete liquefaction of the exudate in red hepatization and unresolved pneu-The exudate in a pneumonie lung which has not undergone resolution is exceedingly poor in cells, and many of the alveoli are plugged with dense hyaline, fibrinous masses. Unresolved pneumonia is, therefore, considered as an acute lobar pneumonia, in which the inflammatory exudate, either because of some disproportion between the leukocytes and other constituents, or because of other causes as yet unknown, failing to autolyze perfectly, cannot be absorbed and hence undergoes organization.

Etiology of the Sleeping Sickness of the Negro.—Aldo Castellani (Cent. f. Bakt. u. Parasit., 1903, Bd. xxxv. p. 62) describes a trypanosoma which he has found in the eerebrospinal fluid of twenty out of thirty-four eases of sleeping sickness investigated in Uganda. In order to demonstrate the parasite, it is necessary to collect about 10 e.c. of spinal fluid, centrifugalize and examine the sediment, when the trypanosoma, at first actively motile, are readily seen. The parasite was not found in the blood, but was discovered in the fluid removed from the lateral ventricles of the brain in two autopsy cases. The cerebrospinal fluid of twelve healthy individuals living in the Uganda district did not contain parasites. The author concludes that the sleeping sickness is in all probability caused by this particular species of trypanosoma.

The Effects of Lymphotoxins and Myelotoxins on the Leukocytes of the Blood and on the Blood-forming Organs.—Bunting (Univ. of Penna. Med. Bull., 1903, vol. xvi. p. 200) finds that the serum of the normal goose is, to a certain extent, toxic for rabbits when injected intraperitoneally or subcutaneously. This toxicity consists in a moderate depletion in the bone-marrow and lymph glands of preformed cells, and to an early and slightly excessive restoration of these elements after withdrawal. The depletion is in large part due to migration of the cells into the peritoneal eavity, during which process the circulating blood shows at first a searcity and later an excess of these elements. slight signs of toxic action are found in the blood-building organs at a distance from the injections. Serum from a goose which had received successive injections of the bone-marrow of rabbits when inoculated into the rabbit gave rise to changes in the white cells of the circulating blood, and to lesions in the hæmopoietic organs in a measure similar to those produced by injections of normal goose serum. The characteristic action of the myelotoxic serum, however, was its marked effect upon the bone-marrow and the cells derived from the bone-marrow. Following injections of this serum in rabbits the circulating blood showed a sharp and marked rise in the total number of amphophile leukocytes, and a less pronounced increase in the lymphocytes, but still an increase above that called forth by injections of normal serum. The blood picture and the histological alterations in the bone-marrow suggested, therefore,

that there had been a sudden and excessive demand upon the bonemarrow for the amphophile lenkocytes. Large doses of the myelotoxic serum produced extensive destruction of the bone-marrow elements "in loco."

Serum obtained by treating goese with the lymph glands of rabbits gave rise to changes in rabbits which differed from those produced by normal goose serum chiefly in the fact that the toxic action of the serum was directed toward the lymphoblastic tissues. The circulating blood showed a primary lymphopænia, followed by a definite and often marked absolute lymphocytosis, while the effect upon the amphophile leucocytes was practically the same as that following injections of normal goose serum. A study of the lymph glands especially made it evident that there was an extensive primary injury to these tissues with a later excessive repair of cellular elements. It was found, moreover, that by increasing the hamolytic power of goose serum for the crythroeytes of the rabbit, the toxic power of the serum for both amphophile leukocytes and lymphocytes of the rabbit was also increased; but these effects were of much less intensity than the characteristic specific changes called forth by injections of the myelotoxic and lymphotoxic sera. Bunting in his conclusions regards lenkocytosis as the excessive reaction of leukoblastic tissue to a leukopenia of the circulating blood, due either to a withdrawal of leukocytes from the circulation or to their destruction within the circulation. The amphophile, cosinophile, and basophile lenkocytes are derived from the bone-marrow, while the lymphoid cells are chiefly derived from the lymph glands and spleen, although the marrow is a lymphoid tissue and contains typical lymphocytes. Amphophile and cosinophile myelocytes may multiply by mitosis, and their number may be increased by the development of specific granules in the protoplasm of large monounclear elements with seant basophilic protoplasm, a cell identical in appearance with the cells of the germinal centres of the lymph glands. Megaloblasts are a constituent of normal marrow and form the proliferating centre of ervthroblastic tissue.

Further Observations on the Agglutination of Staphylococci.—Otto (Cent. j. Bakt. u. Parasitten, 1903, Bd. xxxiv. p. 44) concludes that of the many varieties of staphylococci there is only one which is really pathogenic for man. This variety may be easily diagnosed by its strictly specific agglutinability with the scrum from un animal immunized against the pathogenic variety. The true pathogenic form, furthermore, is alone capable of producing hamolytic staphylotoxin.

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#### . FROM THE PREFACE.

It will be the object of this work to set forth clearly the dangers introduced by venereal diseases into marriage—dangers to the wife, dangers to the offspring, and dangers which come from their morbid irradiations into family and social life—and to indicate the most effective means to prevent these dangers or to limit and circumscribe their spread. This protective duty, which has for its object the preservation of the helpless and innocent from infection, devolves upon the physician in his capacity as sanitarian and gnardian of the public health. The fulfilment of this duty realizes the highest ideals of preventive medicine. In safeguarding marriage from the dangers of venereal diseases, the physician becomes the protector of the wife and mother and the preserver of future citizens to the State.

In the discharge of this responsible duty the physician will find himself confronted with numerous difficulties. The situations created by the introduction of venereal discasses in marriage are many and complicated; the problems presented are delicate, perplexing, and difficult of solution. In dealing with these situations there is required not only a thorough knowledge of these diseases in all their relations, but also a knowledge of human nature, a professional sagacity and a savoir-faire which are not taught in the

Curricula of our medical schools.

It is the purpose of this study to indicate the general principles which should form the basis of the physician's conduct and to formulate as definitely as possible rules for

the basis of the physician's conduct and to formulate as definitely as possible rules for his guidance in dealing with the various situations which may present themselves in ractice.

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-A. H. SMITH, "Specific Medication," Medical Record, March 15, 1902.

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-RICHARDSON, Boston Medical and Surgical Journal, February 5, 1973.

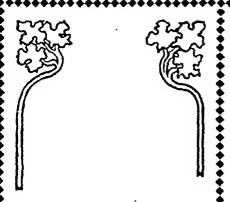
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The specific action of Urotropin in bacilluria has also been proved by Curschmann, Horton-Smith, Gerhardt, Albutt, Cammidge, Marx, Von Schaper and others.

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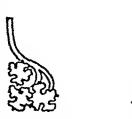
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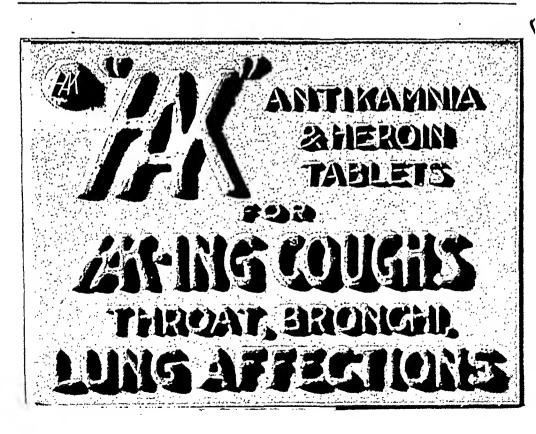
Principal Physician of the Hospital of San Giovanni Calibrita (del Fatebene Fratelli) of Rome—Member of Academy of Medicine, Rome.

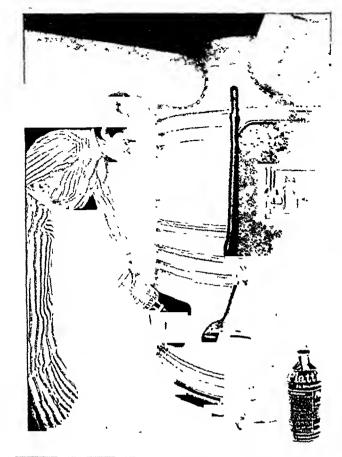
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# AMERICAN JOURNAL. OF THE MEDICAL SCIENCES.

APRIL, 1904.

# THE INFLUENCE OF COMPLICATING DISEASES UPON LEUKÆMIA.\*

BY GEORGE DOCK, A.M., M.D.,
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN.

Investigations in leukæmia during the last decade have led to a great increase in our knowledge of the phenomena of that disease, especially of the minute changes in the blood and tissues. But the gains hitherto have added complexity to the subject by suggesting new problems, instead of clearing up the old ones. Failing the discovery of some microscopic germ as the cause from which the various changes can be traced, the elucidation of many details is likely to be brought about only by patient labor in piling up and analyzing observations.

With this idea I have examined one interesting feature, perhaps I should say one set of features in the disease, viz., the changes following or associated with intercurrent disease. Cases of this kind are rapidly multiplying in the literature, and, having had some instructive cases of my own, it seemed to me that a study of these and others might be useful. I soon found that the outcome would not be as rich as I hoped, but the subject seemed worthy of presentation on account of the nature of the material now available.

I will cite my most important case, leaving out many details of the history:

Case I. Myelogenous (mixed-celled) leukamia; influenza; reduction of leukocytes to 5000 and below; gradual rise of leukocytes six weeks after the complication, reaching 157,000 in another month;

<sup>\*</sup> Read before the Academy of Medicine of Cleveland, September 18, 1903. Vol. 127, No. 4.—APRIL, 1904.

death seventeen months after the complication.—Mrs. C. D. A., aged forty-two years, housewife, was first seen December 29, 1896. From the notes made then I quote: Patient complains of swelling in the left side, shortness of breath, and weakness. The family history is negative as regards ancestors. The husband, who seemed well during the patient's lifetime, developed splenic anæmia a year after her death. (See Transactions of Association of American Physicians, 1903.) The daughter, after the mother's death, had lymphoid hyperplasia in the pharynx and tongue and in the appendix. The latter was the seat of frequent and severe pain; it could be felt as a hard body, as thick as a lead-pencil, through the strong and well-nonrished abdominal wall, and was removed at my advice and found to be free from evidences of inflammation, but with lymphoid tissue unusually developed.

Besides the usual acute infectious diseases, the patient had agne twice in childhood, but does not think she had enlarged spleen, "ague-cake" being a familiar sign in that vicinity at the time.

Menstruation began at thirteen years, and was always regular, except during pregnancy, up to two years ago. Since then the flow has been greater, but pale, and accompanied by bearing-down pains.

At nineteen years she had "dysentery," passing blood with the stools for one month. A series of furuncles on the arms and back followed this. She was then fairly well for ten years, was married, and, except for an abortion after the first pregnancy, remained well until her second and last pregnancy, eight years ago. About the fifth month she had a pain in the abdomen, back, and right shoulder, which closely resembled biliary colic. The patient ascribes all her trouble, however, to the confinement, which was difficult, but the exact results of which do not appear. Three months after it she became intensely jaundiced, and remained so for two weeks. The abdominal pain mentioned above returned then, and at intervals, but without jaundice, up to two years ago.

Two years ago the patient thinks the present disease began, with chilly feelings in the back and hands. In two days there was pain in the splenic region, sore throat, pain in the extremities, and slight fever. The chills lasted for two months, occurring sometimes twice a day, followed by fever and sweating. The pain in the left side continued up to six weeks ago. It was thought to be pleuritic. Three months ago the swelling on the left side was discovered by the patient. It was then about the size of an apple. Soon after the swelling was discovered the chills and fever returned, with paroxysms, usually about 11 A.M. and 2 or 3 P.M., but any exertion was likely to be followed by a chill. The tumor gradually became larger. About two months ago a throbbing pain began in the posterior part of it, and lasted about a month. Then severe and unexplained vomiting came on, and in a paroxysm of vomiting it seemed as if something had fallen in the splenic region. Since then the pain

has been less severe. Shortness of breath on exertion has increased gradually in the last year. There have been no hemorrhages. Headache has been troublesome for some months.

Status prasens, December 29, 1896. Patient is of small size, medium frame, muscles and panniculus well nourished. The superficial lymphatic glafids are not enlarged. The face and visible mucous membranes are of good color, but the hands are pale.

The thorax is symmetrical in the upper part. Examination of the

lungs negative.

The heart is in the normal position; dulness not enlarged. There is a soft systolic murmur all over the heart area; the first sound is

loud. Radial pulse small, quick, regular.

The abdomen is large, especially in the left upper part, where the thorax is also fuller. The recti are separated. The lower edge of the liver is almost at the navel line, but deep in the abdomen. The

edge is thin and tender on pressure.

The splenic dulness begins in the seventh interspace and extends down into the mass below the ribs, evidently the spleen, which can be easily felt as a flattened body reaching to the level of the anterior superior spine of the ilium and to the median line. The edge is thick; there is a shallow notch on the inner side. There is palpable and audible friction over the surface. The patient says the mass is sometimes lower than at present. It is not unusually movable by pressure or position.

There is pain on pressure over the sternum and tibiæ.

The blood is pale, not very thin; fresh preparations show enormous increase of the leukocytes, among which large cells with fine or coarse granules are conspicuous. The blood count shows: red corpuscles, 2,500,000; leukocytes, 367,070; hæmoglobin (Fleischl), Stained preparations show moderate poikilocytosis, many nucleated reds-1:40 leukocytes, or 9074 per c.mm. About onefourth have the size and appearance of megaloblasts, but the two forms run into each other by variations impossible to classify precisely. Differential count of the leukocytes shows: lymphocytes, 0.3; mononuclear neutrophiles, 48.8; polynuclear neutrophiles, 41.6; polynuclear eosinophiles, 0.7; mononuclear eosinophiles, 1.4; basophiles, 2; degenerated, 5. The lymphocytes are often smaller than red corpuscles, but do not show as intense staining of the nucleus as do typical small lymphocytes, and have usually a distinct rim of protoplasm. Many of the myelocytcs have deeply indented nuclei, but the looser, skein-like structure of the nucleus distinguishes most of them from those denominated polynuclear. The eosinophiles, especially the mononuclears, vary much in size from that of a small lyinphocyte to that of the largest mononuclears. The basophile cells are large or small in about equal proportions. The degenerated leukocytes are hard to classify, but seem to represent all the larger forms.

The diagnosis of myelogenous, mixed-celled leukæmia was given, the usual prognosis stated to the husband, and Fowler's solution

recommended to the family physician.

February 1, 1897. The patient entered the medical clinic of the University Hospital. She says that two weeks ago she had influenza, with tonsillitis and coryza. The discharge was bloody, especially in the morning, and a week ago there was moderate nose-bleed. She complains now of great weakness, dyspnæa, pain in the left side, and general itching. She "feels as if walking on sticks."

Status præsens. The patient looks somewhat more anxions than before. The skin is not very pale. The hands feel numb when the arms are fully extended. There is no distinct tenderness over the nerve trunks of the extremities. The tongue is clean. There are no stomach symptoms. The pharynx shows moderate redness and swelling, with seanty mucopurulent exudate. The thoracic organs are negative, aside from a few small rales in both bases on deep inspiration, and a soft systolic murmur over the base of the heart. The abdomen is above the level of the ribs. The edge of the liver is within an inch of the navel line. The spleen extends three fingers' breadth below the margin of the ribs. The lower end is rounded. a shallow notch can be felt just above the point. The spleen is very tender on pressure, freely movable. There is distinct friction over it. The superficial lymphatic glands are not enlarged. There is no cedema of the ankles. The blood count: red corpuscles, 2,540,050; lenkocytes, 7500; Fleischl, 50 per cent. Red corpuscles show marked vacuole formation; many polychromatophiles; some red corpuseles show mitotic figures. The arsenic had been increased up to 12 drops t. i. d.; it was continued, with extract of red bonemarrow (4 e.c. t. i. d.).

February 2d. Red corpuscles, 2,500,000; lenkocytes, 8125;

Fleischl, 50 per cent. Differential counts given in table.

7th. Patient complains of more numbness and also of itching. Arsenic stopped. Temperature has been up to 101° to 101.6° F.;

pulse, 110; respiration, 22.

9th. Red corpuseles, 2,192,000; lenkocytes, 4775; hæmoglobin, 50 per cent. Temperature has not been higher than 99.4° F.; pulse, 80 to 100; respiration, 22. Patient still complains of itching, also of weakness, headache, and slight dizziness.

12th. Red corpuscles, 2,863,000; leukocytes, 5000. The condition remained about the same. The temperature was rarely above normal; there was slight gain in weight. Itching was the most

troublesome symptom.

March 3d. The lenkoeytes number 35,156; red corpuscles, 3,733,333; hæmoglobin, 60. The spleen can barely be felt on quiet breathing. On deep inspiration it extends three fingers' breadth below the ribs. Splenic dulness begins on the ninth rib and is 9 cm. long. On the right side there is dulness from the sixth intercostal

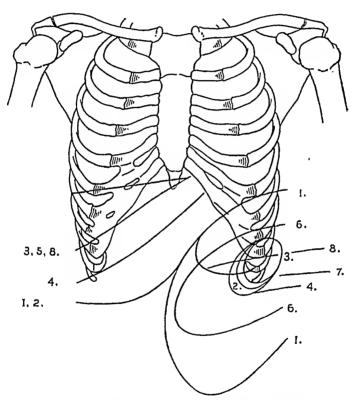
space to an inch above the margin of the ribs and to the tip of the ensiform. The abdomen is slightly distended; no enlarged glands can be felt in it. The inguinal glands are slightly enlarged.

10th. Red corpuscles, 3,125,000; leukocytes, 40,170; hæmoglobin,

55. The systolic murmur over the base is still present. There is

no œdema.

Red corpuscles, 3,100,000; leukocytes, 90,000; hæmo-21st. globin, 70. The patient feels better than before. Has no subjective symptoms. The spleen can barely be felt on quiet breathing; liver not enlarged. Patient has gained eight pounds in all since admission.



Variations in size of liver and spleen at different stages.

April 2d. Red corpuscles, 3,281,200; leukocytes, 157,000.

5th. Patient is going home. Feels very well. Spleen and liver as at last note. Red corpuscles, 3,580,000; leukocytes, 189,000. Continues Fowler's solution.

15th. Red corpuscles, 3,825,000; leukocytes, 217,600. No sub-

jective symptoms; spleen as before; slight ædema of feet.

June 4th. Red corpuscles, 3,600,000; leukocytes, 307,000. Next day, at home, patient had a chill, followed by several others in the next twenty-four hours, and for the next three weeks had a good deal of fever. Severe pain in the splenic region required the use of morphine for sixteen days.

July 1st. Red eorpuseles, 3,600,000; leukoeytes, 307,000. The patient feels as well as before the febrile attack. She has tingling in the toes and fingers; otherwise well. She has gained eight pounds since leaving the hospital. The spleen is three fingers' breadth below the margin of the ribs on quiet breathing; it is hard and thicker than before. The liver is three fingers' breadth below the ribs, the edge thin and of normal consistency. Fowler's solution, stopped during the fever, renewed.

22d. Feels better. Took Fowler's solution up to 10 drops. The hands are better; the feet tingle slightly. Red corpuscles, 3,600,000; lenkoeytes, 178,000. The spleen is slightly smaller. Is now taking boue-marrow.

August 19th. Pain in the legs returned about ten days ago. Began Fowler's solution again, and pain ceased. Looks well; does housework, but tires easily. The liver is not palpable; the spleen is much larger than before, reaching two finger-breadths below the level of the navel; the upper border of dulness in the eighth interspace. Red eorpuseles, 4,000,000; leukocytes, 165,000; hæmoglobin, 70.

October 21st. Patient has been taking Fowler's solution and bonemarrow and is feeling well, and now looks better than she has for a long time. The spleen is smaller, reaching only two and one-half fingers' breadth below the ribs. Red corpuscles, 4,000,000; leuko-

eytes, 57,000; hæmoglobin, 70.

January 27, 1898. General condition has been fairly good. Red corpuseles, 3,095,000; leukocytes, 461,666. The spleen is a hand-breadth below the margin of the ribs, 3 cm. from the middle line. The liver cannot be felt, except on deep breathing; there is dulness to the margin of the ribs. The superficial glands are not enlarged. Fowler's solution continued.

February 26th. General condition is good. Red eorpuscles, 3,533,333; leukocytes, 279,260. Spleen as at last note. This was the last time the patient was seen. April 17th she wrote to say that she was not able to travel, on account of pain in the abdomen and enlargement of the spleen.

June 8th. Reported that patient, who had been trying to come to the hospital, had fever, chills, nansea, and vomiting, and was very

weak. "The spleen fills the entire abdomen."

17th. "Patient is able to sit up, but still very weak. Is entirely deaf and complains of roaring in the ears." Soon after this she died, while I was away from home. An antopsy was made, but no tissues preserved.

Summary of the case: A woman with mixed-celled leukæmia, with greatly enlarged spleen. Two weeks after an attack of what was probably influenza, the leukoeytes were found reduced from 367,070 to 7500, falling to 4775 in two weeks more, with reduction, but not disappearance, of the abnormal white and red cells. The

spleen was much smaller; the liver became smaller later. In two months from the complication the leukocytes reached 40,000, in ten weeks 157,000, and in a year 461,666, having once been as low as 57,000 in the mean time. The liver and spleen remained small for many months, though the spleen was usually easily palpable. For the next six months the patient grew worse in every respect, and died a year and a half after the first observation. The most important stages in the blood are shown in the following table:

Date,	Red cells.	White cells.	Hæmoglobln.	Nuclented red cells,	Small lymphoeytes.	Large lymphocytes.	Transition and large mononuclear.	Polynuelear neutrophiles.	Polynuelear eosinophiles.	Mononuclear eosinophiles.	Myelocytes (Ehrlieh).	Basophile.	Degenerated.
Dec. 29	2,500,000	367,070	50	9074	0.00	0.30	00.0	41.6	0.7	7.4	488	2.0	5.0
Feb. 1	2,541,050	7,500	50									1	}
" 2	2,500,000	8,125	50	2358	4.2	5.7	4.9	70.6			12.3	1	6.0
" 9	2,192,000	4,775	50	1224	2.5	11.8	10.3	56.0		1.4	11.1	1.0	6.0
" 12	2,853,000	5,000		416	1.6	13.3	3.3	63.8	0.3	0.6	9.6	1.0	6.6
March 3	3,733,333	35,156	60	524	0.4	7.6	7.1	66.2	0.2		15.5		2.7
" 10	3,125,000	40,170	55	362	0 15	5.2	24	54.4			20.9		16.4
" ]4	3,125,000	40,370	50	500	0.8	2.4	1.4	62.0	•••••	0.2	29.9	,	3.3
" 21	3,100,000	90,000	50	few	0.1	2.3	3.2	63.7	0.4	0.2	22.3		6.4
Oct. 21	4,000,000	57,000	70	1760	1.3	3.5	7.7	62.0	1.2	1.3	20.8	0.9	23
Jan. 27	3,095,000	461,666	65	7387	2.3	1.3	4.4	63.2	0.4	0.7	27 0		0.7
Feb. 20	8,533,333	279,000	70	6700	8,8	6.0	30	41.0	7.0	0.3	34.0	1.0	5.0

Such a change, more marked than one usually sees in leukæmia under treatment, forces one to try to learn something from it, not only as regards pathology, but, even more imperatively, something of therapeutic value. The most important objective symptom, the excess of leukocytes, disappears. It would seem that by examining such cases one might discover something regarding the production of leukocytes and their appearance in the circulation, as well as their ultimate destruction; also something of the life of the red corpuscles. and of other details of the pathology of leukæmia. It might seem that the process could be imitated, and a symptomatic, if not a causal, treatment be discovered. Medical literature contains a number of such cases, though not so many as one might expect, remembering the vulnerability of the leukæmic to infection. Not only single cases have been reported, but studies have been made, and in the present article I am merely going over ground that has already been traversed by others, my only advantage being due to the fact that I am at present the latest inquirer.

The literature of the complications is unusually confused. Some of the cases have been reported two or even three times by the same or different authors. Besides unavoidable errors, such as those in ages, dates, and other minor details, author's names have been changed. H. Strangways Hounsell, one of the earliest authors, becomes Honsell, Hantell, Strongways, Srangways, and even, by an unnecessary comma, two authors, contributing a case each. Thorsch reported a case in his own name, from the clinic of von Limbeck, and at least two writers ascribe it to "Zeissl," whose name does not appear in the original article.

The subject is complicated by other things. A frequent cause is the lack of exact classification of the leukæmia. In many cases I have been obliged to follow the author's terminology and classify cases that should, perhaps, be otherwise arranged. With future cases this difficulty will become less frequent, and also another regarding the diagnosis of the complication. But owing to the chronic and obscure course of many cases and the tendency of patients to wander from one to another physician, incomplete observations will multiply, and will, nevertheless, often deserve publication.

I shall discuss the cases according to the nature of the complicating disease in the first place, and the variety of leukæmia in the second, and, without trying to follow a scientific order, will speak

first of tuberculosis.\*

### Cases of Tuberculosis and Leukamia.

The combination of tuberculosis and leukæmia was noted very early. Virchow¹ described a case in 1849, and his rival, Bennett,² noted 2 out of 23 cases collected in 1852. Virchow also made the anatomical examination in a case observed clinically by Bamberger³ in 1857. According to Mosler,⁴ there were 12 examples of tuberculosis in the 100 cases of leukæmia analyzed in Martin Ehrlich's thesis in 1872. Yet in the recent literature the combination is rarely mentioned. Many authors admit that they have never seen such a case. It was encountered only twice in the 37 cases observed in the Göttingen clinic,¹¹ with 10 autopsies. Among my own cases, 25 in number, there were no clinical evidences, but in 2 out of 6 autopsies miliary tuberculosis was found, once in a marked degree. I think that more extensive observations will show that the exclusion is not so absolute as has been thought. In my own clinical material leukæmia occurs most frequently in the early part of the fifth decade, when tuberculosis is relatively infrequent. Cornet, Moorehouse, and others have pointed out that this age period is one very prone

<sup>\*</sup> Three articles were received too late to use in this paper. Tommaso Prodi, La Riforma Medica, July 22, 1903, A Case of Lymphatic Leukæmia, with Tuberculosis of the Larynx, Lungs, and Lymphatic Glands. W. J. Susmann, The Practitioner, October, 1903, Tuberculosis in One out of Forty-one Cases of Leukæmia Observed in Various London Hospitals. Wilhelm Neutra, Zeitschrift f. Heilknnde, Band xxiv., 1903, Two Cases of Lymphocythæmia; in one Pleurlsy, with Leukocytes Dropping from 160,000 to 8300; in the other, Suppurative Pleurisy and Peritonitis; Blood Not Thoroughly Examined.

to tuberculous manifestations, but I think the whole subject is one that requires further investigation. This is one of many aspects of leukæmia that can be studied with advantage by the physician in private practice, where the whole course of the disease can be followed. Owing to the nature of the disease patients with leukæmia do not remain in hospitals as long as is desirable for extensive study.

Another fact requires some consideration. Small leukæmic growths closely resemble tubercles. The early literature has occasional mention of leukæmic growths, sometimes of large masses that, especially in the lungs, break down and simulate ulcerative tuberculosis. At an early period Virchow, Boettcher, and Ollivier and Ranvier studied the peculiarities of the two growths, but it was not until the structure of tubercle had been more minutely described by Wagner, Schüppel, and Langhans, and especially after the discovery of the tubercle bacillus, that the differentiation was made certain. It would be interesting to re-examine some of the old museum preparations with reference to the breaking down of such growths. The analysis of cases published before 1882 is very unsatisfactory. The only cases necessary or profitable to examine now are those in

which an effect on the blood or organs has been noted.

There are in the literature about 27 cases that either are cited in this connection or might be referred to. To these I add two imperfect observations not previously reported. The cases of Virchow and Bamberger, mentioned above, throw no light on the question now under consideration. That of Hounsell,5 fairly well described, is of value also only in showing the association of diseases. Besides tuberculosis the patient had scarlet fever, tonsillitis, and secondary pneumonia. The leukæmia was probably acute lymphocythæmia. Ollivier and Ranvier reported the case of a man, aged forty years, with miliary tuberculosis of the abdominal organs, old pulmonary tuberculosis, and leukæmia. The case cannot be analyzed for lack of details regarding the blood. The same difficulty exists in the report by Robin<sup>7</sup> of a case of extensive lymphatic tuberculosis with leukæmia. Still less available is a case mentioned by de Roth,8 of miliary tuberculosis and leukæmia, observed by Knoepfelmacher, but not published. Brueckmann<sup>9</sup> has reported a case of splenicmyelogenous and lymphatic leukæmia with old and recent-tubercles that has some incidental interest, because it appears that the examination of the blood made in a famous German clinic, in 1892, consisted in estimating the proportion of red and white cells in blood, "mit Wasser stark verdünnt." Two cases reported by Volpe<sup>10</sup> are even more imperfectly described, and do not add anything to the material, while several of 6 cases he quotes from the literature are cases of pseudoleukæmia. In a case of Musser and Sailer11 there were "evidences of old tubercle" in the apex of one lung. This and a similar case reported briefly by Saundby<sup>12</sup> show that leukæmia can develop in bodies with old tuberculous foci, as is proved by some

of the cases cited below. Sabrazès<sup>13</sup> has briefly mentioned a case of myelogenous leukæmia and tuberculosis of the lymph glands, with diminution of eosinophiles and mast-cells, and increased polynuclears. The patient reported by Strattmann<sup>68</sup> had a history of apical catarrh and pulmonary hemorrhages before the spleen became large, and may also have been tuberculous. The patient treated with tuberculin by H. Heuck,<sup>64</sup> mentioned below, also had slight signs of pulmonary tuberculosis.

Finally, in Kraus' 32 case, discussed below, there was miliary tuberculosis besides the streptococcus and diplococcus infections.

Of the other 15 cases 7 are examples of medullary leukæmia, with acute miliary tuberculosis. Of these, the cases of Quincke <sup>14</sup> <sup>15</sup> (2 cases), Lichtheim, <sup>16</sup> Schmidt, <sup>17</sup> Bezançon and Weil, <sup>18</sup> and Hirschfeld and Tobias <sup>19</sup> showed diminution of leukocytes as follows:

```
      Quincke, Case 1
      .
      .
      .
      1:3
      to
      1:50

      Quincke, Case 2
      .
      .
      .
      1:4
      to
      1:90

      Lichtheim*
      .
      .
      .
      1:5
      to
      1:370 (250,000 to 8,900)

      Schmidt
      .
      .
      .
      1:2.9
      to
      1:135 (962,000 to 28,000)

      Bezançon and Well
      .
      .
      .
      135,000
      to
      19,871, rising to 45,000

      Hirschfeld and Tobias
      .
      .
      331,000
      to
      110,937
```

In Schmidt's case there were small cavities in the lungs. In Hirschfeld and Tobias' case there were old lesions in the apices, but not cavities, and no clinical symptoms of tuberculosis. The miliary tuberculosis does not seem to have been very severe. No bacilli were found in sections. The leukocytes were as high as 434,000 nine months before the low count, 228,000 four months before, rising to 331,000 two weeks before the low count. Six months later, after a recurring pneumonia, they numbered 283,333, and death occurred five weeks later. In the case of de Roth<sup>8</sup> there was a rise toward the end.

Four cases of myelogenous leukæmia are recorded in which chronic tuberculosis existed, sometimes ending in miliary tuberculosis. These are reported by Elsner and Groat,<sup>20</sup> Sturmdorf,<sup>21</sup> Parker,<sup>22</sup> and Murrell,<sup>23</sup> though the tuberculosis in the latter case may not have been very chronic. In all there was a fall in the number of leukocytes toward the end. In some the lowest count was still so high as to leave little room for doubt as to the diagnosis, viz., in Elsner and Groat's case, 121,000; Sturmdorf's 116,000; Parker's, 100,000, later 130,000; but in Murrell's it was 16,200, from 220,000. Arsenic was freely used in this case.

The other cases show variations in the leukæmic condition and other features that make it necessary to consider them separately.

In the case of Stintzing<sup>24</sup> there was enlargement of the spleen and lymphatic glands, with old tuberculous lesions (cavities) in the

<sup>\*</sup> Elsner and Groat and Hirschfeld and Tobias classify Lichtheim's case among lymphatic leukæmias, but as the author says the polynuclear and mononuclear cells were about equal, I agree with Baldwin and Wilder and Quincke in placing it with the splenomedullary cases, though the lymph glands were also enlarged.

lungs. The leukocytes decreased slightly, 1:100 to 1:150; the glands became smaller, but the spleen remained about the same size. It is difficult to understand the author's statement that the "leukæmia improved while the phthisis made great progress," particularly as the patient died, unless we take a very partial view of the case.

Juenger's<sup>25</sup> patient had enlarged lymphatic glands, and probably acute leukæmia, though the description of the blood leaves some doubt as to its precise character. Miliary tuberculosis of the glands and peritoneum, with early caseation, was found post-mortem. The leukocytes rose from 40,000 to 125,000 in two weeks, two and a half months before death, and fell to 68,800 six weeks before the end, following an attack of diarrhæa. Arsenical pigmentation was then present. The glands became smaller. An abscess in one of them was incised. The blood was not examined again until two days before death, and then showed no excess of leukocytes.

In Francksen's<sup>26</sup> case, probably also lymphatic leukæmia, there was tuberculosis of the lymph glands, spleen, and liver, with final bronchopneumonia. The leukocytes fell from 240,000 to 128,000 between observations four months apart, and did not fall lower in the next three days, or two days before death. The spleen became

smaller toward the end.

Baldwin and Wilder<sup>27</sup> reported a case of probable chronic lymphocythæmia. In this lymphatic enlargement had lasted more than two years, chronic pulmonary tuberculosis, finally developing cavities, as long or perhaps longer. The leukæmia was observed for about two months. There were no recent miliary tubercles. The leukocytes numbered 695,000 at the beginning of the period, reached 1,113,000 nine days before the last count, and then fell to 943,500 and 959,500, without qualitative changes. The lymph glands and

spleen grew smaller four days before the end.

From the available material it appears that chronic tuberculosis does not distinctly influence the eourse of leukæmia, or, as we shall see later, materially influence the leukocyte formula. Acute miliary tuberculosis, on the other hand, is followed by or associated with reduction of the leukocytes in the majority of cases. The exceptional cases may be due to the slight development of the miliary tuberculosis in extent, or to the fact that death occurs before the change has time to take place, though it may be, as de Roth has suggested, that in some eases the body becomes accustomed to the infection and the leukocytes are not affected, as in more acute cases.

Two of my cases, though imperfectly observed, add weight to both

of the first two suppositions.

Case II.—M. T., domestic, aged twenty-five years, first seen June 2, 1896. "She was well until July, 1895, when swellings and red spots appeared on the right leg, and similar lesions appeared on various parts of the body up to the time of examination. The abdo-

men has been large for nearly a year. It was supposed to be due to uterine or ovarian tumor, for which an operation was advised by two physicians she consulted. Weakness present for three months." I found a mixed-celled leukæmia, with red corpuscles, 3,587,500; leukocytes, 598,000; hæmoglobin, 60. There were ecchymoses, up to the size of the palms, on the arms and legs. The spleen extended one inch beyond the middle line, and to the level of the anterior superior spine of the ilium. The liver was not enlarged; the axillary and cervical lymph glands were slightly enlarged, but not the inguinal glands. No pain or tenderness in the bones.

The patient was observed by Dr. Cowie and myself for two years, taking Fowler's solution as steadily as is usually possible. Within three weeks the ecchymosis ceased, menstruation reappeared after an absence of several months, but there was no marked fall in the leukocytes and no noteworthy change in the leukocyte formula. Myelocytes varied from 25 per cent. to 44 per cent.; polynuclears, 30 per cent. to 50 per cent.; lymphocytes, 1 per cent. to 6 per cent.; polynuclear eosinophiles, 1 per cent. to 3.2 per cent.; mononuclear

eosinophiles, 1.2 per cent. to 1.8 per cent.

Becoming anxious for more radical treatment, the patient disappeared from our observation. A year later, three years after the first observation, Dr. Cowie and Dr. Warthin were given an opportunity of making an autopsy by the courtesy of Dr. J. A. Wessinger, who had been called upon in the last illness. The spleen was enlarged; the chief picture was that of a severe tuberculosis of the serous membranes. The blood showed no increase of leukocytes, and microscopic examination of the tissues revealed a complete absence of leukæmic changes, except in the bone-marrow, which was lymphoid.

In this case it is impossible to know when the change occurred. The tuberculosis was more severe than it seems to have been in

many of the reported cases.

In Case III., to be reported more fully on account of other features, a man; aged twenty-nine years, died with so-called lenkæmic apoplexy, without any decrease of leukocytes up to the moment of death. At the autopsy a slight recent miliary tuberculosis was found. Striking as the differences are in these two cases, I think we should await the publication of others before drawing conclusions from them.

## Miscellaneous Injections.

There are 23 reported cases of intercurrent infection other than tuberculosis, including my own Case I. The infections represented are: In medullary or splenomedullary leukæmia: typhoid-like disease (Eisenlohr<sup>28</sup>), afebrile typhoid (Pal<sup>29</sup>), erysipelas (Richter<sup>30</sup>), also reported by Freudenstein; erysipelas, streptococcus, and diplococcus infection with miliary tuberculosis (Kraus<sup>32</sup>), sepsis (H. F.

Mueller,33 Koermoeczi34), empyema (G. Heuck35), influenza (Kovacs,36

Dock), peritonitis (Da Costa<sup>37</sup>).

In lymphatic leukæmia, acute in most cases: sepsis, angina (H. F. Mueller<sup>38</sup>), angina, streptococcus (Weil<sup>39</sup>), streptococcus infection (Wende<sup>40</sup>), sepsis (Cabot<sup>41</sup>), staphylococcus (Fraenkel<sup>42</sup>), colon bacillus (Fraenkel, *ibid.*), staphylococcus and colon (E. Mueller<sup>43</sup>), pneumonia (Oette,<sup>44</sup> Froelich,<sup>45</sup> Thorsch<sup>46</sup>).

Chronic lymphocythæmia was observed complicated by pneumonia by Grawitz<sup>47</sup> and Hart,<sup>48</sup> and bronchitis by Petit and Weil.<sup>49</sup> In some of the cases more than one complication was observed, and

these I shall utilize as far as the data will permit.

The following may also be mentioned: Hensner, in discussing Strattmann's case, mentioned a patient with leukemia in which diminution in the size of the glands and spleen and improvement of the blood followed pneumonia, but relapsed. Rieder (p. 38) has reported a case of medullary leukemia with sepsis, and one of lymphatic leukemia and sepsis, with increase of the leukocytes. The details are too scanty to use. The case reported from Mosler's clinic by Oette may be mentioned here, though I might have included it among the more important cases. A girl aged twenty-three had fever with icterus. The leukemic blood improved after six weeks, and six months later was "almost normal." The case is of great historical interest, and Oette's thesis of much value, but the case cannot now be compared with others. Chantemesse, in the discussion of Bezançon and Weil's case, mentioned a patient of his who acquired erysipelas in the course of leukemia.

Of the cases referred to above, there was a marked decrease of leukocytes to or near normal in 11, viz., those of Eisenlohr, Kraus, Wende, Froelich, Fraenkel (2 cases), Oette, Koermoeczi, Dock, E. Mueller, Cabot. There was a relatively slight fall in 9, viz., those of Pal, Richter, H. F. Mueller, Weil, Thorsch, G. Heuck, Kovacs, Hart, Grawitz. No change or a rise in 3, viz., Mueller, Petit and

Weil, Da Costa.

The cases differ so much in detail that it is difficult to make comparisons. Taking first streptococcus infections, we find that in Richter's case of facial erysipelas following puncture of the tympanic membrane, the leukocytes had fallen on the second day of the complication to 56,000 from the 320,000 of two weeks earlier. The spleen was smaller, and in three days more was 4 cm. less in length, 3 cm. in width. The leukocytes sank to 29,000 on the fourth day, but rose rapidly to 148,000 on the sixth day, along with the development of an abscess of the eyelid and bronchitis, and fell to 52,000 in six more days, while the general and local conditions improved.

In Weil's case of angina with streptococci in the blood, the leukocytes fell during blood infection from 290,400 to 75,682 in four days; seven days later, 66,230. The author thought the angina had in-

creased the leukocytes (the blood had not been examined before), which he estimated at 60,000 to 80,000. I can see no ground for this assumption.

In Kraus' case there was in the beginning a leukocyte count of from 360,000 to 420,000. The complication, a streptococcus and diplococcus infection of the bronchi with miliary tuberculosis, ran a somewhat obscure course, the blood symptoms being the only After slight physical signs of bronchitis, bloodstreaked sputum appeared, with fever and increased size of the spleen. The leukocytes were then 393,400, but fell to 251,600 in about seven weeks, during which there was crysipelas. Two weeks later the count was 240,000. In three weeks they numbered 390,000, in four weeks 504,000. The bloody sputum then contained the cocci mentioned. The sputum then ceased; there were no signs of pneumonia. In three days the leukocytes fell to 120,000, in eight days more to 4600, without myelocytes, mononuclear eosinophiles, mastcells, and nucleated reds, but with many degenerated lenkocytes. The spleen became smaller in the next few days. The lenkocytes rose to 9000; death followed four days after the last count. Autopsy revealed pneumococci in the purulent exudate in the peritoneum and in the spleen and liver, bilateral pneumonia, purulent pleural exudates, pylephlebitis, and tuberculosis of brouchial glands, lung, larynx, peritoneum, and liver. The anatomical diagnosis of leukæmia could not be made. What part the various infections played is difficult to say, but the streptococci do not seem to have been so much concerned as the diplococci. The tuberculosis was probably too slight to be effective.

In one of Pal's cases of medullary leukæmia with bronchitis and erysipelas the leukocytes rose from 75,000 to 105,000 in two days. Tracheotomy was necessary, and death occurred a week later.

In Wende's case, lymphatic leukæmia with streptococcus infection, there was a marked fall, 45,000 to 600.

In Thorsch's case of pneumonia in lymphatic leukæmia (also cited by von Limbeck<sup>51</sup> and sometimes referred to as Zeissl's case) there was a rapid fall in the beginning from 119,000 to 43,500 by the fifth day. Next day there was an extension of the disease, and in three days more the leukocytes rose to 172,000 on the morning of the day of death, 133,000 in the afternoon.

Froelich's case was probably one of lymphatic leukæmia, though the author called it pseudoleukæmia. Under complicating pleuropneumonia the leukocytes fell from 66,667 (having been 309,000) to 8823 in the last week.

In Oette's case of chronic pneumonia the data are insufficient for analysis. He mentions two cases from the older literature showing that bronchopnéumonia does not always alter the blood picture in leukæmia, as it had in his own case.

In chronic lymphocythæmia 2 cases have been reported compli-

cated by pneumonia. In that of Grawitz the leukocytes, "already rather low," sank lower in the beginning and rose to a considerable height in defervescence. There was no change in the formula. In Hart's case there was a fall of from 1,168,000 to 450,000 on the

fourth day of pneumonia. Death occurred two days later.

The 2 cases of influenza cannot be compared with accuracy, because in 1, my own, the diagnosis was based on the anamnesis only. In Kovacs' case the leukocytes, only 67,000 at the highest count, though they had been higher, apparently, fell to 17,000 eleven days later. Six days later there were 33,000. The patient also had bronchitis, pneumonia, and otitis. In one of H. F. Mueller's cases the patient gave a history of influenza, not observed by the author, with diminution in the size of the enlarged glands, which regained the original size after the fever subsided.

The various cases reported as examples of sepsis complicating leukæmia cannot be compared with advantage, but some of them have points of interest that deserve mention. One of the first was the case of H. F. Mueller.38 A man with lymphatic leukæmia, with 180,000 leukocytes, had a subperiosteal abscess in the right leg. count made then, three weeks after the former one, showed 400,000 leukocytes. The glands were about a third their former size; the spleen was also smaller. Death ensued four days after the last count. In Cabot's case of sepsis in lymphatic leukæmia there was a sudden fall from 40,000 to 5661 in one week, and a progressive fall to 471 in nine days more. In Koermoeczi's case of myelogenous leukæmia with sepsis, originating in the nose and leading to hemorrhagic pericarditis without bacterizemia, the lenkocytes fell from 100,000 to 2000. In H. F. Mueller's case of myelogenous leukæmia there was sepsis following abscess from therapeutic injections. The leukocytes had already fallen from 406,200 to 246,900, influenza having been passed through. They then fell to 225,000 with the onset of sepsis, and in the following seven weeks reached 75,500. Pleurisy and pneumonia then developed, and ante-mortem, eighteen days after the last count given, there were 57,300 lcukocytes. The spleen was smaller in the later stages; the leukæmic character of the blood was

In both of Fraenkel's cases of acute lymphæmia, one of staphylococcus infection, the other colon infection, there was a marked fall from 123,000 to 600 in twelve days, and 220,000 to 1200 in sevendays.

In E. Mueller's case of acute lymphæmia with streptococci, staphylococci, and colon bacilli in the exudate in the pharynx, the leukocytes fell from 109,600 to 6800 in five days, 39,200 in the last twenty-four hours.

In Eisenlohr's case of typhoid-like infection, the leukocytes, enormously increased before, fell to almost normal. An attack of follicular angina was followed by an increase, which did not subside in the remaining four weeks of life.

In Pal's case of afebrile typhoid there was a fall from 991,000 to 650,000 in sixteen days, most of it in eight days. Death occurred a week later. Pal could not see that the typhoid infection (not suspected during life) had any influence on the blood or other clinical phenomena. Besides the typhoid there was jaundice, and a traumatic, suppurating hæmatoma.

In G. Heuck's case of empyema there was a variation of from

400,500 to 80,100, rising after thoracotomy to 169,800.

I have already mentioned H. F. Mueller's case, in which the leukocytes increased during infection. Two other similar cases have been recorded. In the case of Petit and Weil there was chronic lymphocythemia. Broughitis occurred, fatal on the sixth day, after diminution of the enlarged glands. The leukocytes increased in the period from two days before bronchitis to the last day from 202,238 to 398,866. Da Costa<sup>37</sup> mentions a case of splenomedullary leukemia, in which, within ten days after the onset of peritonitis, the leukocytes rose from 245,000 to 400,000.

The cases just cited are of importance chiefly in a suggestion they offer. In all three the rise of leukocytes was discovered early in the complication; the patients died soon after. It is possible, of course, that a fall might have occurred after the rise had the cases ended less abruptly. The earliest period after complication has rarely been carefully observed and should be thoroughly studied in future.

From the foregoing it appears that in the great majority of cases intercurrent infections cause a decrease of the leukocytes in leukæmias of various kinds. The fall may be so slight as to leave the gross picture of leukæmia unchanged, but in about half the cases the white corpuscles fall to normal or below. It is interesting to note the extreme leukopenia that occurred in some cases: 600 in one of Fraenkel's, 1200 in another, 600 in Wende's, 471 in Cabot's, 2000 in Koermoeczi's.

Besides the leukocyte decrease, the organs, enlarged as the result of the leukemia, became smaller. In some cases the organs became smaller later than the fall of leukocytes (Quincke<sup>14</sup>), sometimes earlier, in others simultaneously; sometimes the organs became smaller without diminution of leukocytes (H. F. Mueller, Petit and Weil). The diminution was sometimes very rapid. Quincke estimated the change in the volume of the spleen in one case at 100 grams a day, a loss that I think must have been exceeded in my own case. It is often difficult to distinguish between this change in the organs and that observed in some cases of leukemia a short time before death. Sabrazès mentions a case in which cutaneous neoplasms became smaller during a terminal infection, but from the original report\* I cannot see anything peculiar, especially as the patient was taking arsenic and quinine at the same time.

<sup>\*</sup> Listran, J. Contribution a l'étude de la leucocythémie aigue, Thèse, Bordeaux, 1893, p, 66.

### Changes in the Red Blood Corpuscles.

Changes in the red cells have not been studied as carefully, perhaps, as they deserve in complicated leukæmias. Out of 18 cases in which the reports are full there was a rise in the number of red cells, simultaneous with the fall of leukocytes, in 8. The difference was often slight, but in 6 it was 500,000 or more (once 1,300,000) per cmm. (Lichtheim). In the other cases the risc was insignificant, or there was a fall. The latter was 500,000 or more in 4 cases; in 1 1,200,000 (Juenger). The great variations in the red count in leukæmia without complications should be borne in mind. A difference of a million or more may be observed in a short time independent of visible causes. The frequency of the rise in the red cells, while the leukocytes and other symptoms seem to indicate the opposite process, suggests a change in the blood fluid as the cause. The fact that 4 cases with marked risc occurred in tuberculosis (Lichtheim, Schmidt, Sturmdorf, de Roth) is interesting, but the cases do not offer a satisfactory explanation. Quincke noticed the unusual bloodlessness for leukæmia, post-mortem, in 1 of his cases. second case of tuberculosis the vessels were unusually full of blood.

The histological changes in the red corpuscles are interesting, but variable. Nucleated red cells are not always absent, as some have thought. In Richter's case they appeared during the complication. De Roth noticed many, including some in mitosis. In Juenger's case they were pretty numerous, but disappeared two days before death. In my case these cells were less numerous than before the complication, and increased as the leukocyte count regained a high point, but there were many, even at the lowest period, and often in mitosis. The condition of the red corpuscles should be carefully observed in future.

## Qualitative Changes in the Blood, Especially in the Leukocytes.

The earlier observers were unable to notice the finer details in the cells, on account of the lack of methods. Mueller mentioned, in reporting his first case, that mitotic cells (myelocytes) disappeared almost entirely, and the leukocytes changed, so that the leukemia seemed better, judging from the blood. Mueller's second case, with increase of the leukocytes, has often been misquoted. He himself admitted that no accurate examination of the blood cells had been made. He thought there might have been an increase of polynuclears, as occurs in sepsis, but he also thought the new cells might have been derived from the shrinkage of the enlarged glands, in which case they would hardly have been polynuclear.

Kovacs noticed in his case of influenza with slight decrease of leukocytes that the myelocytes disappeared almost completely, the eosinophiles also, the mitotic cells and nucleated reds completely. There was an increase of polynuclear cells, so that the blood picture was that of lenkocytosis. With the rise of lenkocytes the marrow elements reappeared.

Fraenkel noticed no increase of polynuclear cells in his first case, in which, however, the examination was not thorough. In his second case all varieties were reduced.

Richter observed disappearance of mononuclear cells during the complication, with increase of polynuclears up to 90 per cent., the latter in the secondary rise with abscess. Before the complication the two classes had been about equal.

Thorsch, whose case appears to have been chronic lymphocythæmia, with mononuclear cells about 97 per cent., and no eosinophiles or nucleated reds, says that the changes were: mononuclears, 138,600; polynuclears, 1400 at one extreme and 40,585 to 4915 at the other, showing an absolute increase of polynuclears. But this was by no means such an increase as would cause distinct leukocytosis in a non-leukæmic subject, and before the complication, with 113,000 leukocytes at one time, there were 4520 polynuclears. Thorsch suggested that relative increase of polynuclear cells is observed by all in complicated leukæmia, and he made H. F. Mueller's case one of the number, but, as I have shown above, without sufficient basis. Hirschlaff\* has a reported case showing that the polynuclears can increase markedly in leukæmia without infection.

In Lichtheim's case of tuberculosis with a fall of 250,000 to 8900, there was a relative increase of polynuclears, viz., from 50 per cent. to 90 per cent., which would amount to a slight increase above normal, but far below the polynuclear count at the height of the leukæmia.

In Baldwin and Wilder's case, without marked alteration of the blood count, there was no notable change in the leukocyte formula.

In Koermoeczi's case of sepsis, with a fall of from 100,000 to 7300, the eosinophiles, myelocytes, and mast-cells disappeared. The polynuclear neutrophiles numbered 75 per cent. (possibly 70 per cent.; there is an error in the report). Just before death counts of 3000 and 2000 were made, with slight increase of the lymphocytes, but no other change.

Adler<sup>32a</sup> examined the blood from Kraus' case, with special reference to the leukocyte formula. Kraus had reported disappearance of the myelæmic condition and the appearance of degenerated leukocytes. Adler shows in tabular form the fall and ultimate almost complete disappearance of the mononuclear neutrophiles (25.50 per cent., 100,514 cells to 0.40 per cent. and 18 cells), the complete disappearance of the basophiles and mononuclear and polynuclear eosinophiles. In the rise before the final fall there was an increase of lymphocytes and decrease of eosinophiles. The eosinophiles disappeared completely with the beginning of severe septic phe-

<sup>\*</sup> Deutsche med. Wochenschrift, 1898, Vereins-Bellage, p. 162.

nomena, and the lymphocytes (small) increased to 40.80 per eent.; large lymphoeytes, 1.80 per cent.; mononuclear neutrophiles, 0.40 per cent.; polynuclear, 58.80 per cent., the latter being only slightly increased relatively.

Bezançon and Weil noticed in their ease of tuberculosis that the leukocytosis was polynuelear during the infection, instead of mononuclear; basophiles, mononuclears, and eosinophiles were few. There were no nucleated red cells, whereas before there were many, some of them in mitosis. Later, as the infection advanced, the leukocytes rose again (from 19,871 to 45,500), and myelogenous eells, with nucleated reds, increased. In the case of Petit and Weil there was no notable change in the formula. In the case of Weil the polynuclear cells were relatively as well as absolutely diminished; the eosinophiles also.

In Elsner and Groat's ease there was an increase of polynuclears and lymphocytes, relatively, and a diminution of myelocytes, as the tuberculosis advanced. But not only in the number of leukocytes, at the lowest 121,000 cells, but also in the formula, the leukæmic character was preserved: polynuclears, 68; myelocytes, 17.5; lymphocytes, 6.5; eosinophiles, 5.2; many normoblasts and megaloblasts.

Sturmdorf observed in his case, in which the number of leukocytes was not much altered during the observations, that each rise in temperature was accompanied by an increase of polynuclears and decrease of myelocytes, "suggesting an intercurrent leukocytosis."

In Wende's case, with a drop of from 45,000 to 600 leukocytes, there was an increase of polynuclears of from 3.4 per cent. to 10 per cent., and a decrease of lymphocytes from 95 per cent. to 88 per cent. in nine days. There are some discrepancies in the author's

figures, but they do not materially affect the statements.

In the ease of Hirschfeld and Tobias, with a fall only to 110,937 (from 424,000), the polynuclear eells were not relatively inercased; the myclocytes were lower then than when the count was above 400,000, but higher (11.5 per eent.) than when it was 300,000 (7.6 per cent.), and there were other variations, but as the author shows, by the counts of another leukæmic patient, the variations were no greater in the case of infection than are sometimes observed without it.

In Murrell's case there was a marked fall in the number of myeloeytes, though the differential counts are unusual and cannot be readily compared with others. For example, the cosinophiles are given as 20 per eent. with counts of 20,000 and 29,000; none with 16,200; besides which it is said the myelocytes, 20 per cent., 44 per eent., and 7 per eent. on different days, were chiefly eosinophile.

Parker states that in the low count, 130,000, the polynuclears were relatively fewer than at the height of the leukoeytosis, 70.8 per cent. and 57 per ecut.; the myeloeytes high, 25 as compared with 14; the

other forms not notably altered.

risen to 35,000.

Hart found no noteworthy changes in the blood in his case of lymphocythemia.

Grawitz noticed no change in the formula, either in the fall in the beginning or the rise after the pnenmonia or after a turpentine abscess with temporary low count.

In my own case the polynuclears were relatively and absolutely about the same as in normal blood. The lymphocytes were relatively and absolutely about normal, relatively higher than in the high stage, but absolutely slightly lower. The polynuclear eosinophiles were relatively and absolutely low, the mononuclear cosinophiles relatively lower than before, but still considerable, and even higher relatively than at later periods with excessive leukocytosis. The (Ehrlich's) myelocytes were relatively and absolutely low, but even at the lowest count, 9.6 per cent., higher than is usually found in any accidental myelocythæmia. Mast-cells were relatively as in other stages. Degenerated leukocytes were relatively about as high as in the first observation, but higher than they became later as the count rose. Nucleated red cells were relatively much higher than before, reaching 1 to 2.4 at one time, or absolutely 2000 per c.mm. One-fourth were megaloblasts, and a few of these were in mitosis. Nucleated reds were absolutely more numerous at the first count, 1 to 40, or 9074 per c.mm., with a few in mitosis. A few myelocytes also were in mitosis. The reds showed poikilocytosis, vacuoles, and variations in size, as well as the control of the control rystals formed notable changes from the earlier c in blood kept for several weeks, and not until the leukocytes had

During the rise of leukocytes that began between two and four weeks after the fall was discovered the formula was altered by the relative decrease of lymphocytes, the relative increase of myelocytes, and a slight relative increase of eosinophiles of both kinds. The nucleated reds increased slowly. The large number of these cells during the low leukocyte stage is exceptional. It is possible that they were fewer or absent in the preceding two weeks immediately after the infection, and that they began to reappear in the stage of reaction, but the counts do not support this view.

It appears, then, that the changes in the lenkocyte formula are not uniform, though there is a disposition for the lenkæmic character to disappear more or less completely under the influence of infections, and for the polynuclears to increase absolutely as well as relatively.

#### When Does the Change Occur?

When the change occurs is a question that cannot be answered very fully, on account of the small number of cases in which the process could be observed from the beginning.

In Eisenlohr's ease the glands and spleen diminished daily from

the beginning of the infection and the blood changed simultaneously. As the glands and spleen enlarged again, the blood resumed its former leukæmic character. The decrease lasted fourteen days. One month after the decrease the blood showed proportions of 1 to 4.

In Kovacs' case the blood resembled that of leukocytosis nine days after the beginning of the infection. In twelve days the spleen was smaller and softer. On the tenth day there were few myelocytes; no nucleated reds. Three days later there was an increase, with many myelocytes, and in three more there were 33,000 leukocytes.

In Fraenkel's first case the whole process took place in twelve days. In his second one the leukocytes had fallen to 47,000 by the

seventh day, 3800 by the eighth day, 1200 by the tenth day.

In Richter's case the leukocytes fell from 56,000 to 29,000 in two days, but two days later they were 148,000, and six more 52,000.

In Thorsch's case the lowest point was reached in four days.

Death occurred three days later.

In Lichtheim's case there was a slow and steady decrease for two months, when death occurred.

In Koermoeczi's case, eight days after a count of 100,000, the leukocytes had fallen to 7300. The patient lived five days longer, with almost the same blood picture.

In Kraus' case the leukocytes fell quickly after infection, viz., from 120,000 to 4600 in one week. In five days more the leukocytes had increased to 9000, and in four more the patient died.

In Weil's case the fall from 270,000 to 75,682 took place in six

days; in seven more the number was 66,230.

Elsner and Groat noted a gradual fall of 200,000 leukocytes in three months.

In Wende's case, sepsis in acute lymphocythæmia, the leukocytes fell in nine days from 45,000 to 1600. In Cabot's case the fall to subnormal took only sixteen days; in E. Mueller's case five days.

In Murrell's case there was a fall in three days of from 150,000 to 20,000. Then an increase six months later, and another fall from 167,000 to 16,200 within five weeks.

In my own case of influenza the fall of from 367,070 to 7500 probably occurred within two weeks, but there was no actual observation in that time.

In general, the fall occurs soon after the infection, more promptly in acute than in chronic infections. The cases of chronic infections, however, are too few and too diverse in character to enable us to draw sweeping conclusions. There are also too few cases observed from the beginning to ascertain the first effects of the infection (or intoxication). Perhaps these differ in various cases.

As regards changes in the formula, Hirschfeld and Tobias give a table showing that variations can be observed in the leukocyte formula quite apart from complications, especially notable in the polynuclear and myelocyte count. This will be confirmed by all who have followed up cases of leukæmia for some time, while changes in the gross number of cells, both red and white, are equally common, and often quite as much or even more marked than in some of the cases examined above.

A very interesting fact brought out in some of the cases, and one that I observed with particular care in my own, is the rapid rise of the leukocytes after a fall to normal, and with a great decrease in the size of the previously enlarged organs. Actual observation must, of course, be the final test of such a matter, but it is easy to understand how a chronic leukæmia may have a sudden increase of circulating leukocytes, including cells not found normally in peripheral blood, or how a so-called pseudoleukæmia may become leukæmic within a short time. These observations do not throw any light on the process by which the new cells get into the peripheral vessels, but they prove that a long time is by no means necessary for a great excess of leukocytes to appear in the peripheral capillaries.

The Effects of Various Processes Other than Infection on Leukamia.

Finding such striking effects on the leukocytes from the influence of infectious disease, one naturally asks whether other diseases or intoxications may not have similar consequences.

Oette<sup>44</sup> studied the effect of fevers on the course of leukæmia, at the instigation of Mosler, as long ago as 1879, but he was limited by the greater obscurity then surrounding both fever and leukæmia,

and did not materially advance the subject.

Freudenstein<sup>31</sup> re-examined it in 1895. He gathered many interesting facts regarding the fever of leukæmia from the early literature, besides the histories of ten of the earliest cases of infection studied here. He concluded that fever is a frequent (63 per cent.) but not constant symptom of leukæmia, and ascribed this to substances derived from broken-down leukocytes, but did not study the possible results of such processes on the leukæmia itself, doubtless because of the difficulties surrounding such an investigation.

Marischler<sup>52</sup> reported a case of lymphatic lenkæmia complicated by a Grawitz tumor of the right kidney. There was repeated hæmaturia, considered at first as a result of the lenkæmia, but later more properly ascribed to the renal tumor. The lenkocytes fell from 96,000 October 16th, 84,000 November 25th, to 48,000 on February 27th, and then rose to 72,000 on the last day. The polynuclears rose from 15.60 per cent. (or 21.70 per cent. at the beginning of the hæmaturia) to 57.60 per cent. The mononuclears fell from 82.30 per cent. (or 76.20 per cent.) to 40 per cent. The difference was still more marked in the blood of the last day. The changes were, therefore, qualitative rather than quantitative. Marischler explained the changes as due less to the hemorrhage than to the carcinoma toxin, a view I do not think free from error. Marischler

gives theoretic reasons, based on experiments, for his view, but the passage of a necrotic bit of tissue, 1.5 cm. by 0.25 cm., shows that the explanation by changes following loss of blood is very near. The author gives the literature of new-growths complicating leukæmia, the only genuine cases he could find being those of Whipham and Lannois and Regaud. In these no effect of the cancer upon the leukæmia was noted.

The literature of leukæmia contains references to cases in which reduction of leukocytes had taken place under the most diverse drugs, such as iron, arsenic and its salts, phosphorus, quinine, oxygen, etc.; but it is suggestive that the drugs that some have found most valuable have failed entirely in the hands of others, without perceptible reasons in the cases themselves. Most of the reports give such scanty details of the blood in the stage of recovery that they cannot be utilized at present. The literature is largely available in the study of Vehsemeyer.<sup>53</sup>

The first to report a careful study of the process were Toulmin and Thayer,<sup>54</sup> who noticed a fall of from 714,000 to 7500 leukocytes in twenty-three days in a patient taking arsenic. Two weeks later there were 9500 leukocytes. The leukocyte formula changed from:

Lymphocytes					0.96	to	6.9
Polynuclear					70.0	to	83.2
Transition .				٠.	3.0	to	2.5
Eosinophiles					2.3	to	3.0
Myelocytes .					23.5	to	4.0

showing a relative increase of lymphocytes and polynuclears. The myelocytes, though much reduced, were still notably high, 4 per cent.

Bramwell<sup>55</sup> mentions a case in which the leukocytes fell from 210,000 to 1600 in thirty-eight days under treatment with arsenic, CO<sub>2</sub>, and oxygen, and remained below normal for a month. Therewas fever and an eruption from unknown cause, so that the case, perhaps, should be included among the infections. The formula was altered as follows:

			Sept. 28,		Oct. 9.	Oct. 15.	Oct. 21.	Nov. 4.	
Polynuclear				69.0	70	91	75	62	
Myelocytes				26.5	25	3	5	7	
Lymphocytes				3.5	5	5	20	31	
Eosinophiles				1.0	1+	1+	0	0	

Cabot<sup>56</sup> and d'Allocco<sup>57</sup> have reported cases in which the leukocytes fell to normal or below, but, at least in the former case, myelocytes were always present, and in a degree that would in itself excite the suspicion of leukæmia, or, in the absence of acute symptoms, suggest some serious disease of the bone-marrow requiring careful observation.

McCrae,<sup>58</sup> however, published a case in which there was not only no leukocytosis, but no sign of medullary disease. A man, aged twenty-eight years, had medullary leukæmia with a blood count in

the spring of 1898 of 2,680,000 red cells, 584,000 leukocytes. He was put on arsenic, and in August there were only 184,000 leukocytes, and the spleen was barely palpable. In September there were 9250 leukocytes. Arsenic was continued, but in November the leukocytes numbered 178,000. In December there were 98,000; in April, after taking 10-drop doses of Fowler's solution, 5000 per c.mm. The myelocytes numbered 20 per cent. to 23 per cent. in the high stage, but were absent in the low one. The polynuclear leukocytes were 86 per cent. with 9250 leukocytes, normal with 5000. Mast-cells were present only once, in the relapse. Nucleated reds were absent after the first fall.

Taylor<sup>50</sup> has reported 3 cases in which the excessive leukocytes disappeared under the influence of arsenic. The improvement lasted for months, and then relapsed in all eases. A second stage of improvement followed in all; in 2 a third. The changes were qualitative at first, and varied both in quality and quantity at different times. In 1 case all qualitative changes disappeared, and a slight lymphocytosis was the only evidence of blood disease. In the other cases myelocytes persisted to the extent of 1 per cent. to 3 per cent., part eosinophilic. Taylor's discussion of this subject can be read with advantage by all who carry out experiments in the treatment of leukæmia. As in the ease of infections, the low leukocyte count does not ensure recovery from the disease. This is shown by many reported eases, including the remarkable one of Saundby,<sup>12</sup> in which the white cells dropped from 540,000 to 8000 in cleven days, but death occurred in coma some weeks later.

It must be remembered that many of the patients whose cases are eited in the early part of this study were taking arsenie, sometimes in large doses, yet I think no one will ascribe the changes wholly or even in part to the drug in all cases. I may add that personally I have never seen a fall below 50,000 leukocytes in leukæmia from arsenic, but in only a small proportion of my eases was it possible to

push the drug as it should be.

Under other drugs besides arsenie changes have been observed in the blood count in leukæmia. Von Jaksch<sup>60</sup> treated a patient with thyroiodin and cupric arsenate and noted a fall of from 295,000 to 560,000 to 28,000 in thirteen days, the blood at the latter count giving the picture of leukocytosis with few nucleated reds. The liver became smaller, even before the leukocytes fell. For five weeks the leukocytes were not above 100,000, but in six days reached the former high figure and remained there. Thyroiodin was also given during the rise. The formula two days before the lowest count was: polynuclears, 74.04 per cent.; mononuclear neutrophiles, 10.71 per cent.; polynuclear cosinophiles, 0.70 per cent.; mononuclear cosinophiles, 0.35 per cent.; small lymphocytes, 14.55 per cent.; large lymphocytes and transitional, 3.70 per cent. Basophiles were few at all times, and absent in the earlier examinations.

Pollitzer<sup>61</sup> reported a case of acute leukæmia, in which the leukocytes fell from 91,875 to 8500 in the course of seven days, while the patient was taking quinine in gram doses; fever continued; the spleen grew smaller. The patient died twenty-three days later. Postmortem the picture was that of acute anæmia gravis with lymphoid hypertrophy of the spleen, intestinal tract, bone-marrow and lymph glands. The author attributes the effect to the quinine, but the fever and the fatal termination suggest that it was due to something else, either an intoxication from the products of cellular break-down or an infection.

In another case of Pollitzer quinine was used in 1.5-gram doses with a rise and subsequent fall, leaving the leukocytes higher than before. The author cites a case of Kuehnau and Weiss, <sup>62</sup> in which a patient with Hodgkin's disease was given pilocarpine and developed acute leukæmia. Sabrazès says that in a case of leukæmia with malaria quinine injections had a happy effect, not only on the malaria, but also on the course of the leukæmia.

Richter and Spiro63 treated a patient with splenolymphatic leukæmia and apical tuberculosis with cinnamic acid. Intravenous injections of very small doses of this caused the leukocytes to increase within three hours from 170,000 to 560,000. There was also a slight increase of red cells. Polynuclear cells increased from 45 per cent. to 86 per cent.; mononuclears fell from 55 per cent. to 14 per cent.; eosinophiles, scanty before, increased, and nucleated red cells appeared, but the increase of leukocytes soon disappeared. twenty-four hours the original number was reached; four days after the first injection the number was 46,000, and it then gradually rose to the former point. The process was repeated in two more injec-The spleen and lymph glands grew smaller; the general symptoms improved. The author points out that the experiment shows how much more intensely the diseased hæmatopoietic organs react to irritants than do normal ones, and he compared the results of his experiments with those in some of the cases studied in this paper.

A number of observations have been published on the action of organic extracts and bacterial products upon the leukæmic subject.

H. Heuck<sup>64</sup> at an early period gave tuberculin injections in a patient with leukæmia, who had slight signs in one apex, but no bacilli in the sputum, and no reaction to 5 milligrams of tuberculin. Doses of from 10 to 120 mg., in nineteen injections, caused reactions like those in phthisis. From the twelfth injection (60 mg.; the leukocytes were not counted before) there was a fall in the number of leukocytes each time, quickly returning, though not quite to the previous number; so that at the end of the observation the proportion was 1 to 48 instead of 1 to 57. There was general improvement, with diminution in the size of the glands.

Pal<sup>29</sup> also used tuberculin in a leukæmic patient, and noted a slight

decrease of leukocytes after six hours, followed next day by a rise. In three days the number was 154,000 in place of 134,000, and the glands were larger, but the leukocytes fell to 103,000. A week later with 135,000 leukocytes the polynuclear cells were increased, the temperature and subjective symptoms worse.

Beitzke<sup>65</sup> 15 used tuberculin in 6 leukæmic patients in Quincke's The results were very uncertain, the injections not being continued long enough to permit conclusions to be drawn and other treatment being carried out at the same time. Two patients that gave most distinct evidences of improvement were taking arsenic.

Pollitzer gave tuberculin in a case of medullary leukæmia in doses of 2 to 200 mg., without reduction of leukocytes, but with increase in the size of the spleen and more marked cachexia. In a case of lymphatic leukæmia tuberculin was given for two weeks in doses of 2 to 64 mg., with a gradual but slight rise of leukocytes, without change in the formula.

Nuclein (Horbaczewski's) was also used by Pal in the case mentioned above, with a fall of leukocytes, but with enlargement of the glands. Pal purposely avoided marked reactions in his experiments, in order to prevent severe effects on nutrition. Pollitzer also used nuclein in both cases cited above. In the first 2-gram doses given for five days had no effect. In the other case there was a slow and immaterial fall, followed by a rise.

Jacob used splenic extract in a patient with leukæmia, giving it subcutaneously at intervals of two to four days. The injections were followed by sweating, anxiety, and dyspnœa, symptoms that Jacob had observed in animals treated with organic extracts, and which he attributed to a leukocyte congestion of the lung capillaries. There was a slight rise in the number of leukocytes, after the early injections, followed by a fall to about half the number present before the experiment was begun. As there was an increased excretion of nitrogen in the urine, Jacob also concluded the injections increased the breaking down of leukocytes.

Here may be mentioned Franke's attempt to use an extract of leukæmic glands. A packet of glands from a case of lymphatic leukæmia was rubbed up with physiological salt solution and kept Injected into rabbits in doses of 5 c.c. to 10 c.c. there were evidences of breaking down of leukocytes. On account of the patient's condition the treatment could not be carried out as intended.

From these few experiments we learn little more than the need of others, and also something of the practical difficulties of such experiments. The blood must be examined at short intervals after the treatment is given, differential counts must be made, and an almost limitless range of work may be found in studies of the cytolytic conditions at various stages. The careful observation of the body and the subjective symptoms and studies of the metabolism, as shown by the urine, are also desired,

There are still other cases on record that illustrate possibilities in leukæmia.

Strattmann<sup>68</sup> reported a remarkable case, in which a patient with enlarged spleen and leukocytes and red corpuscles in equal proportions underwent an exploratory operation on the supposition that the enlargement of the spleen was due to malignant disease. After considerable manipulation of the spleen for diagnostic purposes, and following massage of the organ in order to overcome possible bad effects of the manipulation, the removal was abandoned, and the patient made a good recovery, so that not only was the spleen smaller, but the blood count was 5,300,000 red corpuscles; leukocytes, 1500.

This may be contrasted with Parker's case, referred to in the early part of this paper. In this a patient with old tuberculosis and enlarged spleen, but negative blood count ("the large lymphocytes seemed more numerous"), was explored, with a view to removal of the spleen. Soon after this the blood was markedly leukæmic.

Here we may allude to Senn's<sup>69</sup> interesting case of leukæmia "cured by Roentgen rays." The symptoms of intoxication, such as high temperature, make one wonder whether there was an intoxication from the absorption of broken-down products of spleen and blood, or, perhaps, an accidental infection, and reports of other cases treated by the same method will be awaited with interest. It is to be hoped also that in such reports the blood will be fully described.

A full and satisfactory explanation of the changes observed in leukæmia under the influence of other diseases does not seem possible at present. We are still too much in the dark regarding the cause of leukæmia, the nature of thechanges in the tissues and the mechanism of the blood changes, and we are only beginning to learn something of the effects of infection and intoxication on the blood-forming organs and the circulating blood. The work done by Muir,<sup>70</sup> <sup>71</sup> Dominici,<sup>72</sup> Werigo and Jegunow,<sup>73</sup> Rubinstein,<sup>74</sup> Lengemann,<sup>76</sup> Roger and Josué,<sup>76</sup> Weil,<sup>77</sup> Flexner,<sup>78</sup> Bunting,<sup>79</sup> and others opens up a most promising field, but at present does not go far in explaining the difficulties in this particular subject.

An early and natural explanation was that diseases associated with leukopenia, or without leukocytosis in ordinary cases caused in leukæmia a decrease of leukocytes. This might apply to miliary tuberculosis, or typhoid fever, such as Eisenlohr's case was supposed to be. But further reports not only opposed this view, but even led to the opposite one, viz., that diseases ordinarily causing leuko-

cytosis have an antagonistic effect in leukæmia.

Ortner<sup>80</sup> offered a plausible explanation, viz., consumption of the body, due to infection, but Beitzke pointed out some important objections. It does not account for the altered leukocyte formula often observed; the change sometimes comes on early, before the exhaustion of the body is evident; at other times leukæmia shows

advanced wasting and cachexia without notable change in the leukocytes. H. F. Mueller's theory is attractive chiefly because of its obscurity. He suggested an "alterative" action, but in the present state of our knowledge this does not explain anything. The leukocytolytic theory of Fraenkel is also attractive. It seems borne out by the author's observations on degenerated leukocytes in his own cases, and the increased excretion of uric acid. It seems analogous to the rapid disappearance of certain tumors, some of which (sarcomata) closely resemble leukæmic growths, under the actions of poisons like arsenic, or those of certain infections, as erysipelas. Recently the chemotactic theory has become more prominent, and has received the support of Ehrlich, whose influence in the study of leukæmia is deservedly so great. Quincke's objection, that no evidences of transfer of leukocytes are present, might be explained by a rapid breaking down of the cells.

It seems to me the process in most cases is complex. Breakdown and consumption must occur in cases with severe cytolytic poisons, and in some must preponderate. In others chemotactic processes will be most important, and innumerable variations in the clinical course and the blood picture will probably depend partly on the kind, extent, and intensity of the intoxication, partly on the histological peculiarities of the new-growths, and the capacity of their cells to enter or be poured into the circulation. Thus, in acute lymphatic leukæmia, the changes will not be the same as in the chronic myeloid

alteration of all the blood-forming organs.

Finally, the question as to therapeutic bearings must be met. It is easy to understand how many have looked upon the changes observed in cases cited above as evidences of healing. The most striking sign of lenkemia, the excess of leukocytes, disappears, and sometimes the spleen and lymph glands return to their normal size. Yet that the change is not wholly favorable appears from the fact that no case has really recovered. Most patients died while still under the influence of the process that was thought to have healed them, and, although some seem to have had their lives prolonged, none have lived longer than many leukæmics without such complications.

Weil has suggested that the action of the complicating infections is too "brutal," and this may be so, although the cases hitherto observed show considerable variation in severity. But, considering the hopelessness of the ordinary treatment of leukemia, it seems that carefully planned experiments, either with bacterial products or organ extracts, might show a more safe and permanent result. I need not go into the details of such experiments, but may point out the necessity of thoroughness of the observations as an essential. Previous experience with the substances to be used, either on men or animals, is desirable, while a familiarity with the methods of blood examinations is indispensable.

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#### CARCINOMA OF ABDOMINAL CAVITY; PUNCTURE OF INTESTINE DURING PARACENTESIS ABDOMINIS; PRESENCE OF CARCINOMATOUS FRAG-MENTS IN ASCITIC EXUDATE.

#### REMARKS ON CYTODIAGNOSIS.

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THE following ease is of interest as showing the difficulty of diagnosis of abdominal disease, the danger of even the most earefully performed paraeentesis, and the value of microscopie examinations of exudate, etc.

Mrs. B., aged sixty-eight years, complaining of abdominal distention, dyspnœa, indigestion. Family history unimportant; acute Bright's disease twelve years ago, with apparent complete recovery as far as symptoms showed. Six months previously the patient noticed abdominal enlargement, which, being naturally corpulent, she attributed to fat, discovering soon, however, that fluid was present. Fluid increased, persistent discomfort after feeding developed, and, later, diarrhœa. The urine was markedly diminished, albumin and easts were present, and the patient became steadily weaker.

Examination revealed only ascites, hidden somewhat by a thick apron of fat; liver dulness present, as far as could be judged, in normal extent; ædema of legs, loud systolic apical heart murmur,

slight dulness and few moist erepitations at base of lungs.

Patient had been tapped one month previously, eleven quarts of dark fluid being removed, a considerable amount of fluid blood

eoming away at finish of operation.

At the second tapping (the first while in our hands) twelve quarts of a bloody fluid were removed; no free blood flowed; liver dulness did not appear quite as extensive as normal; patient seemed much relieved after operation, and gastrie symptoms abated.

Ten days later a third tapping brought away six quarts of fluid resembling that of the previous tappings, some gelatinous and granular material coming away just before removing the cannula.

The operation in each case was performed by a surgeon, local cocaine anæsthesia and incision through the skin between the navel and pubes preceding the introduction of the trocar; little if any pain was experienced by the patient; a large apron of fat reaching to the pubes interfered greatly with the drainage of the abdominal cavity.

In six hours after this (third) operation there was a complete collapse; temperature previously, 99° to 100° F., dropping to

97° F.

Tympanites developed quiekly; abdominal pain and vomiting, rapid, weak pulse, and rising temperature made us suspect a bowel perforation and subsequent peritonitis. Death took place in three days. At no time after the first appearance of fatal symptoms did the patient's condition seem to justify any further exploration of the abdomen, and, as the examination of the fluid and material removed made the presence of cancer probable, such steps were deemed inadvisable in any case.

The elinical pieture in this ease was from the first obscure; the huge accumulation of fat present in the abdominal walls precluded any satisfactory examination; at times, even before twelve quarts of fluid were removed, fluctuation was indistinct; there was no anæmia, the withdrawal of so much fluid into the peritoneal cavity causing, in fact, a distinctly concentrated condition of the blood, as is sometimes seen; cirrhosis of the liver or careinoma of some abdominal or pelvie organ were considered the most probable causes of the recurring ascites and associated symptoms.

The bloody appearance of the first fluid removed was suspicious of malignant or tubercular disease; neither suspicious cellular elements nor bacilli were to be detected. The second fluid removed

was, on the contrary, suggestive from the outset. The colloid-looking lumps in the precipitate passing ready formed through the cannula must necessarily have been fragments of some tumor formation or material direct from the intestine; as a matter of fact, both substances were present. Further examination showed specific gravity, 1020; albumin, about 0.3 per cent.; sngar, 0. Microscopically fibrin, intestinal material, starch, vegetable fibres, meat fibres, and some bunches of leptothrix (proving that the bowel had been punctured) were readily seen.

The puncturing of the intestine in paracentesis abdominis, although always considered a real danger, must be considered as infrequent; in this case more than usual care had been taken; it is possible, of course, that portions of the intestines had become adherent in

some part and presented resistance to the trocar.

The cellular elements in the exudate attracted our attention from the outset; quite numerous red blood cells were, of course, to be seen; distinct pus cells were few; on the other hand, epithelioid cells or cells resembling the larger lymphocytes were numerous, either single or grouped as in the drawing (4), showing fibrillar intercellular structure, and columnar cells in groups (3), evidently parts of distinct glandular structures, were in evidence. The arrangement and variety of these first-mentioned cells cannot be said to be diagnostic of carcinomatous conditions; similar-looking cells are present in tubercular exudates; their presence in masses, as in the figure, was suggestive and suspicious, more from its gross appearance than from the character of the individual cells; the distinctly glandular-looking cells, arranged in columns (3), could only be intestinal or from adenocarcinomatous new-growth.

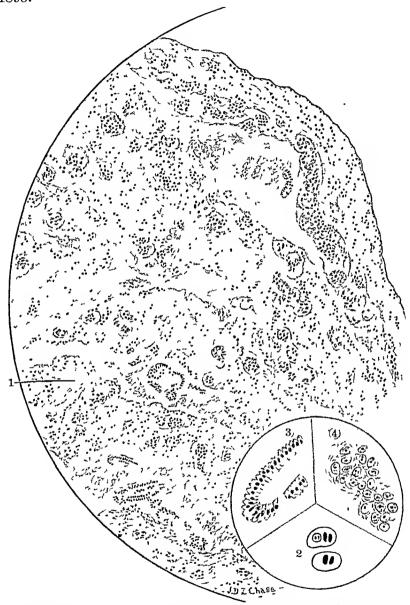
The colloid masses referred to, on being teased out, gave the picture as shown in the figure and just described; it seemed certain thereafter that the cells of the exudate were the colloid elements. Hardened and prepared the colloid masses gave the picture shown in the drawing (1), which can be briefly described as "adenocarcinoma showing advanced colloid degeneration," probably from the suggestive follieular structures connected with the intestine.

The diagnosis of malignant disease in various parts of the body, by means of the character of the cells found in the exudate, has been for some time a rather fruitful field of speculation. We are at present, however, much nearer an accurate working knowledge on the subject, thanks to the careful work of Dock and others; but the readiness with which the earlier writers in the carlier microscopic days accepted various atypical cellular modifications as evidence of malignant disease is striking.

Quincke considered cells of large size in any number, either separate or grouped, as most suggestive; the presence of the glycogen reaction was considered to make the diagnosis almost certain.

Eichhorst makes the statement that "especially in cancer of the

pleura we find in the exudate not rarely abundant fatty granular cells and cells with multiple nuclei," which are characteristic of cancer. Geigel and Voit were practically in accord with this view in 1895.



1 Fragment of tumor removed during paracentesis. 2. Cells and cell inclusion from a case of carcinoma recti 3 and 4 Types of cells and arrangement found in fresh exudate.

Rieder, in the same year, in a detailed and well-illustrated article, is distinctly of the opinion that polymorphonuclear endothelial cells, cells showing atypical mitoses, vacuoles, and having a tendency to appear in clumps, are certainly malignant. Neelsen agrees with this view.

The description and illustrations of the cellular findings in malignant and other exudate, as given by Dock several years later, show clearly that these views must be taken cautiously, since all the cellular changes described by the observers as characteristic of malignant exudates were found by him in conditions distinctly not malignant, although, as he admits, in much smaller numbers.

Dock agrees with Rieder as to the possibility of distinguishing cancerous from tuberculous exudates from a consideration of the cellular constituents thereof. In the latter, as a general rule, according to both observers, the great variety of cells, the mitotic and amitotic figures are rare; a small cell, with the general characteristic

of a lymphocyte, being more usually scen.

Warthin a few mouths later reports the ready diagnosis of a primary sareoma of the pleura from the large number of spindle cells found in the exudate; these spindle cells differed rather materially from the ordinary fibroblast found in pleural exudate in not showing branching processes and in their regularly more oval-shaped nucleus; numerous symmetrical mitoses were also present. A comparison of these cells with those present in serous and fibrinous pleural and pericardial exudates and with normal pleural cells does show, in the gross, some difference, but certain characteristics are possessed by all. The great number of the spindle cells is probably the most suspicious character of the exudate in his case.

Hemmeter insists upon the regularity with which cells showing mitotic figures, symmetrical and asymmetrical, may be found in the

washings from eases of carcinoma of the stomach.

A more complete microscopic picture and a certain diagnostic feature is presented in eases in which (as in ours) tumor fragments are removed during the simple operation of paracentesis or lavage. The reported instances of this happening are not numerous.

Steiner, Ricder, and Lenhartz give instances of recovery of tumor

particles from aseitic fluid.

Prentess, Girvin and Steele found partieles of malignant growths in pleural exudate; the fixed and stained specimens usually have shown very distinctly the nature of the new-growth; examination of the fresh partieles is not always so certain, the cellular structure not being so clear. Ordinary small endothelial cells or lymphoid cells entangled in the fibrin coagulum of simple or tubercular exudates can present suspicious features when examined in the fresh state. Our own experience in cytodiagnosis has been of more or less interesting nature. In our cases of simple or supposed tubercular pleurisies it has been easy to demonstrate the preponderance of the lymphocyte-like cells described now as the most common cell in these conditions. The large endothelial cells, at times mononuclear, at times polynuclear, were regularly seen in small numbers.

In several fluids from spinal punctures, in which no pneumococci or other micro-organism could be demonstrated by stain or culture, but which were also negative for tubercle bacilli by inoculation, the

same lymphocytc-like cell was the prevailing element.

No exudates due to the more common organisms, streptococcus, pneumococcus, or typhoid bacillus, have come under our observation since this paper was begun. It is now generally found that in such exudates the pus cell, the ordinary polymorphonuclear cell, is in excess.

In a gclatinous, chocolate-colored sputum from a patient with persistent cough and wasting, we were struck by the almost purely cellular condition of the material. Closer examination showed a total absence of the ordinary polymorphonuclear leukocyte, and the presence of such dense numbers of mononucleated round or oval lymphoid-like cells as to give the idea that one might be observing an extremely cellular tissue, such as sarcoma, rather than an exudate or secretion. These cells stained readily when fresh, were nongranular, the size of a medium-sized or large lymphocyte; no mitoses or multinucleated elements were made out; nucleated stains showed a reticulated, well-formed nucleus. The findings of the subsequent autopsy were given to be a "tumor of the lung." A further application of the cytodiagnosis was shown in the case of a patient suffering from an intermittent diarrhea, associated with bloody, mucus-like discharge. Numerous mononucleated and multinucleated cells of cpithelioid character were demonstrable, and were in themselves suggestive of a condition other than a simple inflammatory one, but the most suspicious elements were cells such as pictured in the drawing (2), with their cell inclusions. The association of these bodies with carcinoma and their supposed parasitic nature is now a matter of every-day discussion, and needs no comment.

I do not know of their being described previous to this in exudates, etc. Proctoscopic examination and subsequent history revealed

malignant ulceration of the upper rectum.

We were singularly unfortunate in our cases in not being able to demonstrate mitotic figures, and hence the question of the diagnostic value of these figures in the cells of exudates cannot come into consideration. Steiner failed to find mitoses in his case. dition of the new-growth, whether rapidly growing or not; various physical states, such as serous membrane irritation, probably account for the presence of these figures. I must agree with recent observers "that the presence in exudates of many cells showing mitosis will, in most cases, allow us to make a diagnosis of malignant. discase;" such cells are certainly rarely present in other conditions, and then but in scant numbers. Small cells grouped in masses, as shown in the drawing (4), are suspicious, and were enough in our case to convince us of the malignant nature of the trouble. does not often find such groups in simple conditions, nor could one readily explain their presence in such; masses of desquamated endothelial cells do not show the intercellular fibrous strands as in the figure; moreover, the large size of the endothelial cells would

show their nature. Large, multinucleated, endothelial-like cells are more common in malignant disease, but are seen frequently in other conditions.

Cells of such glandular type and arrangement as found in our case, and pictured in the drawing (3), could not be passed over. In this instance not only the nature of the new-growth, but its situation or the situation of incustatic accidents is demonstrated.

One of our recent cases is of interest, and, at the same time, shows the limitations of cytodiagnosis. In this instance, a few days after an operation removing the right breast for what has been shown to be a cancerous degeneration of an adenofibromatous tumor, a pleural effusion, with fever, developed. Repeated aspirations (3) were necessary to relieve the patient. Subsequent metastasis, developing rapidly along the incision, led us to consider the condition as probably due to extension of the disease to the pleura. The fluid of the various tappings showed at no time, however, any cells suggestive of cancerous vegetation. On the other hand, the preponderance of 98 per cent. to 99 per cent. of small mononuclear leukocytes was always evident. There has been no reaccumulation of fluid since the last aspiration eight weeks ago, the fever falling to normal after the first and remaining there. The cellular condition in this instance is suggestive of a tubercular more than a malignant or mechanical pleurisy.

One must certainly admit that considerable information and help may be derived from careful examination of exudates, etc., as to their cellular constituents. The presence of cells in any number should lead to more careful consideration of their type, arrangement, and nuclear condition.

In a majority of instances one may suspect malignant disease if large numbers of nuclear figures, typical or atypical, are present; their absence, on the other hand, by no means, excludes the possibility of malignancy. Occasional nuclear figures are to be found in other conditions.

Endothelial cells with many nuclei are probably but not certainly more numerous in cancerous exudates. Cells of exudate tending to appear in bunches or groups with intercellular fibrillæ (as shown in 4) are, to a degree, suspicious; apart from fragments of squamous epithelium and desquamated flakes of large endothelial cells, there are few conditions which would cause cells not of these varieties to appear in compact masses. Small groups of lymphocytes or pus cells, of course, are often seen.

Unusual cells of glandular or other type, or such as are depicted containing cell inclusions, must be given a significance of their own. The question of cytodiagnosis of tubercular and other exudates has been of late freely discussed, and it seems probable that tubercular exudates are more or less regularly associated with lymphocyte-like cells, particularly after the first few days.

Mechanical exudates show more often numbers of large endothelial cells, often in large plaques, the "placards" which Widal and Ravant consider pathognomonic of mechanical exudates or transudates.

Infectious pleurisies, etc., are found to have the polymorphonuclear leukocyte as the characteristic cell of their exudate.

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# THE CLINICAL BEHAVIOR OF THE LYMPH GLANDS IN TYPHOID FEVER.

## By DAVID L. EDSALL, M.D., of philadelphia.

So far as I can determine by examining the most important recent works on typhoid fever and by searching through any papers with suggestive titles, the statement that widespread enlargement of the lymph glands, recognizable clinically, occurs in typhoid fever has not been made. It is known that the lymphatic enlargement found at necropsy is not limited to the tissues in the intestine and to the glands in the direct path of the lymph stream from the intestine. Post-mortem findings of enlargement of the inguinal and the periœsophageal glands are sometimes noted; and lymphatic tissues that are even as distant from the intestines as are the tonsils occasionally show enlargement, and in some instances are probably directly involved in the typhoidal process. Indeed, typhoid fever plays its part so largely in lymphatic tissues that it is to be expected that it should, at times, produce widespread glandular enlargement, readily recognizable at post-mortem, particularly since the disease is well known to be a general bacterial infection and not a local process.

Clinically, however, in cases in which it is necessary to distinguish between typhoid fever and other diseases in which glandular enlargement is common, the discovery of many readily palpable glands is usually accepted as being a point in favor of the last-mentioned class of diseases and against typhoid fever.

In May, 1903, in the course of my services at the Episcopal Hospital and at St. Christopher's Hospital for Children, I encountered within two weeks 3 cases of rather peculiar nature, in which glandular enlargement was a point of some importance in the diagnosis. The first case was in a boy aged six years. In the course of typhoid fever, and while rötheln was prevalent, this child developed a rötheln-like rash and was found to have easily palpable glands in the occipital and the anterior and posterior cervical regions, as well as in the axilla and the groin; and subsequent observation showed that these glands exhibited a slight further increase in size and a distinct increase in number. The absence of any other new symptoms, the fact that the fever was dropping at the time and continued to decrease, the lack of any influence upon the patient's general condition, and the rapid disappearance of the eruption, without any trace of desquamation, led me to decide that this was merely an accidental rash.

In the second case, that of a boy, aged eighteen years, the presence of swollen and slightly ulcerated gums, with some excess of leukocytes, and with an absence of any distinctive evidence of typhoid fever, suggested the possibility of an early acute leukæmia. This patient showed a small number of readily palpable anterior and posterior cervical, axillary, and inguinal glands; and within a few days the palpable glands were found to be increasing in number, though not distinctly increasing in size. He soon developed spots and a Widal reaction, however; the leukocytosis disappeared, and he rapidly settled into a course of typical typhoid fever, no complication,

except the mild grade of stomatitis, being discovered.

The nature of the third case still remains somewhat obscure, although I believe it was typhoid fever. In considering the possibility of syphilitic fever in this case, I found easily palpable anterior and posterior cervical, axillary, epitrochlear, and inguinal glands. The man denied the possibility of syphilis, however, and showed no primary lesion, and he had no subsequent manifestations of that disease. While he had no absolutely characteristic evidences of typhoid fever, that diagnosis remains the most probable.

These observations led me to make notes at various periods of the disease in a series of cases of typhoid fever. As a result, I think I may state without hesitation that in a considerable number of cases widespread glandular enlargement that is, to be sure, slight, but sufficiently marked to be discoverable clinically, occurs in this disease; and in some instances the glandular enlargement is as marked as that which usually occurs in certain other infectious diseases, and is usually looked upon as somewhat distinctive of those diseases.

The regions that I especially observed were the groin, the axilla, and the anterior and posterior portions of the neck. In some cases the condition of the epitrochlear and the brachial glands was also noted. In most cases the enlargement observed was very slight; it was sometimes so slight that I doubted whether it could be considered to be actual enlargement. The most common condition was the appearance of many glands about the size of buckshot or a little larger; these were, as a rule, especially easy to palpate in the axilla and the groin. Little attention was paid to such a condition of itself, as I appreciated the fact that glands of this size might readily have been present from the beginning and have become apparent only because of emaciation. Very frequently, however, I noted, during the course of the disease, the development in the axilla and the groin of glands that I have described in the notes as varying in size from that of small peas to that of hazelnuts, while in the neck they were often noted as being of the dimensions of small peas. In some of these instances such glands were present in small numbers on admission, but I noted a distinct increase in their number during the course of the disease. As a rule, the occurrence of glandular enlargement could be determined only by painstaking and deliberate examination; occasionally, however, it was sufficiently marked, especially in the axilla and in the neck, to be apparent upon rather hasty palpation. In the groin the conditions were not quite so patent, because most of these patients, as is so very common, showed here some old enlarged glands in the beginning; hence a little more care was necessary in this region, in order to determine whether these glands were enlarging and whether new ones were appearing.

I am, for several reasons, disposed to be very guarded in using my figures as to the frequency with which enlargement can be noted. In the first place, the number of cases that I have observed is too small to be distinctive. In the second place, the circumstances attending the observation of such cases are likely to lead one astray; that is, typhoid fever patients usually emaciate rapidly during the course of the disease, and then rapidly put on flesh after convalescence has begun. In consequence of this, glands already palpable would become more distinctly so; and others, not at first palpable, would appear as the result of the emaciation; while, when fat is being reacquired, the conditions are reversed. This tends to give one the impression that the glands are showing slight chlargement during the course of the disease, and that this enlargement is disappearing during convalescence. Furthermore, anyone that makes a practice of searching for small lymph glands will agree with me that in the most varied conditions a few may often be found high up in the axilla, while they are somewhat less easily and less frequently discovered in the anterior and posterior cervical regions, though common here. Naturally, also, the more frequently the search is repeated, the more often will glands be discovered and the greater will be the number found; hence, repeated search at various periods of the disease might give one the impression that the glands are increasing somewhat in number, when this is not the case. I have been careful to exclude, as far as possible, these sources of error,

and have weeded out from the positive group the cases in which I thought that the notes of increase in the size or the number of the glands might have been due to mistakes in observation; but even after having done this, I am inclined to think that my figures show

a greater frequency of the condition than is quite correct.

The total number of cases that I observed was about 60. Some of them, however, were seen only late in the course of the disease; and another group exhibited complications like furunculosis. The conditions in the former were not distinctive, and in the latter any glandular enlargement might readily have been due to the secondary infection. I have, therefore, excluded all these cases. This brings the total number down to 43. Of these, 7 at the time my service ended were still in such an early stage of the disease that the behavior of the glands during the course of the disease could not be determined properly, so that the cases in which satisfactory notes have been obtained number only 36.

In these 36 cases I observed the occurrence of glandular enlargement during the course of the disease in 25 instances; in 4 the conditions were doubtful, and in 7 there were no determinable changes in

the glands.

At the time of admission, 12 of these 25 had enlargement of the peripheral glands other than the inguinal; they likewise had inguinal enlargement, but, of itself, this is, of course, of little interest. Twelve showed no enlargement of other glands than the inguinal, and in 5 of these cases no inguinal enlargement could be observed. Three of the last-mentioned 5 cases occurred in young boys. In the 1 case remaining of the 25 I have no notes made upon admission.

Notes during the course of the fever show that in 22 of the 25 cases there developed distinct enlargement of the axillary and the cervical glands; in 1 other case glandular enlargement, noted upon admission, distinctly decreased before the fever ended, while in the 2 remaining cases the condition of the glands was doubtful during the course of the fever. Although these 2 cases last mentioned were doubtful at this period, they are included among the positive cases because, in early convalescence, it was determined that there had been a decided increase in the size and number of the glands.

Upon discharge, 16 showed a distinct decrease in the glandular enlargement; in 6 it persisted about as it had been when last noted; in 2 there was, as mentioned, a distinct increase in the size of the glands, and in 1 the axillary glands were noted to be decreased and

the cervical increased.

Of the 7 cases mentioned in which the notes covered too brief a period to allow of their inclusion in the above figures, 1 showed distinct decrease in the glandular enlargement within a week after admission (he had been ill twenty days when admitted), in 2 there seemed to be a distinct increase in the size of the cervical glands, and in 4 the notes were absolutely indistinctive.

While I have stated that I am not convinced that enlargement occurred in all the cases in which my notes indicate that it did, I have no question concerning most of the cases that I have included as positive, and there were certain cases in which the changes in the glands were so readily determinable that there could be no possible source of error in the observations. There were, for instance, three boys, aged between twelve and fourteen years, that upon admission showed, after the most careful search, no enlargement of any glands, except for a very few, about the size of buckshot, in the inguinal region. During the course of the disease these patients all developed many palpable glands, a few of the largest becoming the size of small hazelnuts, many reaching the dimensions of moderatesized peas, and numbers of buckshot-sized ones becoming palpable. In two of these boys the glandular enlargement decreased decidedly during defervescence, even before the patient was being fed more freely, and hence before any flesh was being put on; and in both these patients the enlargement had practically disappeared before their discharge from the hospital. In the third case the enlargement, although it decreased somewhat, persisted until the time of discharge.

There were also several cases of relapse in which changes in the glands could easily be followed. In one of these it was noted that upon admission the inguinals only were enlarged. Within a week the cervical, axillary, and epitrochlear glands had become easily palpable. Two weeks afterward, when the patient's fever had disappeared, the glands were found to have decreased markedly in size and number. Ten days later, after he had been for a week in a relapse, the enlarged glands were found to be much more numerous than they had been in the primary attack; and the number of these glands continued to increase up to the time of his discharge, which was somewhat premature. (Two weeks later, just after I left the

service, this man was admitted in a second relapse.)

In another case there were no notes upon admission; but during the course of the disease the inguinal, axillary, and cervical glands were felt in moderate numbers and were the size of peas. At the end of an afebrile period of a week the axillary and the cervical glands had decreased greatly in size; the inguinals remained unchanged. Toward the end of a relapse of two weeks' duration the axillary and the cervical glands were found to be again as large as peas or larger, and to be much more numerous than they had been before. These glands had decreased to the size of buckshot before the patient's diet was increased, and remained in this condition at the time of his discharge.

In a third relapse-case only slight glandular enlargement, if any, could be determined to have occurred during the primary attack, while during the relapse there was distinct and general enlargement.

Notes were not made with sufficient frequency during the course of

these cases to determine definitely when the enlargement occurred. In some instances it seems to have appeared early in the disease, for a number of patients were admitted at the end of the first week with a large number of palpable glands, and this enlargement disappeared late in the course of the disease or during convalescence, indicating that it had been due to the attack of typhoid fever. In most instances, however, the enlargement appeared to develop—most strikingly, at least—in the latter part of the disease; and in a number of cases increased enlargement or the first definite enlargement was noted during early convalescence. As already indicated, it had, in the majority of cases, disappeared to a greater or less extent before the discharge of the patient, but in about one-quarter of them it persisted unchanged up to the time of discharge.

I at first thought that by carefully observing the glands it might be possible to learn some facts that would be of value in diagnosis. It seemed possible, for instance, that this might afford some help in distinguishing between typhoid fever and obscure cases of tropical malaria. There were a number of such cases in the wards during this period, and in 2 of these repeated searches for the plasmodium, even when instituted by a person so skilled as is Dr. Ghriskey, failed to show the parasites; although they were ultimately discovered. The glands in these patients were observed persistently, but showed

no enlargement.

It likewise seemed possible that in acute tuberculosis glandular enlargement would occur less commonly and less rapidly and would not be widespread. Two cases of acute pneumonic tuberculosis were observed during this period in the ward; they showed no general glandular enlargement. Perhaps in disseminated tuberculosis and some other conditions the enlargement of the glands might be of interest in the diagnosis. On the whole, however, I believe that it is of little consequence in this way, for the enlargement in typhoid fever tends to occur late, and frequently so late as to be, for this reason if for no other, of no diagnostic importance; and it is also often so slight that it can scarcely be of much help. Furthermore, I do not believe that slight enlargement of the lymph glands, such as I have described as occurring in typhoid fever, can be of great importance in distinguishing this condition from other infectious disenses, for I am convinced that glandular enlargement occurs much more frequently in many infectious diseases than the common descriptions of these diseases would lead one to believe. This has recently been clearly shown by Schamberg to be true of scarlet fever and also of measles; and there is certainly a growing recognition of the fact that glandular enlargement is common in many of the other bacterial infections.

The possible bearing of the glandular enlargement upon prognosis has interested me somewhat, because, as I have already stated, the enlargement was in most cases observed rather late in the disease, a fact suggesting that it might have something to do with the pro-

duction of immunity, instead of being merely an expression of general infection of the lymphatic apparatus with typhoid. The 43 cases that I have referred to all recovered, so that I can make no direct statement as to its possible bearing upon prognosis. During the time that these observations were being made there were three deaths from typhoid fever in the wards; but all these patients died of severe complications that had no direct connection with the severity of the typhoid toxemia, and all these cases have been excluded from the list-two because they had furunculosis, and the other because I had no notes until toward the end of the patient's life. It is possible that more careful and more extended observation will show that the degree of the glandular enlargement may be made to influence the prognosis. This is, at any rate, suggested by the fact that the enlargement occurs most markedly as convalescence is approaching, as well as by the fact that the most marked enlargement of the glands was observed in several of the mildest cases. Furthermore, the behavior of the glands in several cases of relapse suggests this possibility. As stated, a limited glandular enlargement was observed in a number of cases during the primary attack; while during the relapses, which were followed by definite recovery, a much more marked enlargement occurred. The last-mentioned fact, however, indicates that glandular enlargement, unless quite marked and general, cannot have any important bearing upon prognosis, for readily discoverable enlargement may be followed by relapse.

I thought that the development of decided glandular enlargement, together with the usual signs of approaching convalescence, might afford some indication that the disease is actually about to terminate, and might be helpful in recognizing early the not uncommon cases in which the afebrile state is but slowly established or the disease is much prolonged. It cannot, however, prove of great importance in this way, as is indicated by the conditions just mentioned in connection with relapse; a recognizable and fairly considerable glandular enlargement may certainly occur, and yet be followed by

a distinct relapse.

These observations concerning prognosis were suggested by the extensive discussion in recent years concerning the tissues active in the production of immunity. The behavior of the glands in the cases that I report has a certain degree of interest in this connection, although, of course, a limited one. The fact that the glandular enlargement occurred so generally in cases that ended in recovery and that it developed late in the disease, as convalescence was being established, seems to suggest that the lymphatic tissues were active in these cases in establishing immunity, and thus to add some support to the view that the lymphatic tissues play an especially active part in this function.

The chief interest in these observations, however, lies in their relation to diagnosis. Glandular enlargement, unless very marked,

cannot be considered a strong point against typhoid fever, for enlargement of the degree that is, for example, usually seen in syphilis is not very uncommon in typhoid fever, and a somewhat lesser degree is very common.

## RENAL DISEASE OF PREGNANCY AND RETINITIS ALBUMINURICA.

WITH REPORT OF A CASE.

BY LEO JACOBI, M.D., of NEW YORK.

Many systemic manifestations of pregnancy are situated on the border line between the physiological and the pathological. Vomiting, cedema, hypertrophy of the heart, nervous disturbances, etc., are all illustrations of a fluctuating equilibrium. Still more important are the renal changes accompanying the condition, and these have, in the course of time, given rise to abundant discussion and discord; naturally enough, for no fixed line of demarcation can be traced between the normal and the pathological. Neither should this non-plus us, if we only recollect the gradual character of all fundamental transition, as between life and death, animal and vegetable, and many another.

It is granted by all that certain changes are found in the kidneys of the pregnant woman; but divergence of opinion begins the moment we ask, Are these changes organic and abiding, or merely functional and transitory? The practical bearing of the answer needs no emphasis, and yet a definite answer is not forthcoming.

Equally deplorable is the obscurity prevailing in respect to that most important result of renal disturbance—albuminuric retinitis—occurring in pregnancy.

The writer does not presume to deal exhaustively with these formidable problems. He wishes merely to report an interesting

case and to indulge in a few warrantable inferences.

Mrs. Dora M., aged thirty-three years, a large, strong, and well-built woman; has been married thirteen years. The first conception took place soon after marriage. In the third month of this first pregnancy she sought the aid of a midwife, who performed criminal abortion. Since that time the patient suffered from a chronic inflammatory gynecological affection, for which she underwent repeated courses of treatment at home and abroad. Conception did not occur again for eight years, in spite of varied therapeutic measures directed to that end.

Four years ago she again went abroad, and her husband seized the opportunity for acquiring syphilis. He presented himself with a chancre and was properly treated from the start. He has remained

well, at least to all appearances.

The wife returned soon after his infection, and, in spite of all admonitions, sexual relations were resumed. What seems to be noteworthy, the woman, who had been sterile for eight years, now conceived promptly. Though she never showed any manifestations of infection, the baby was born prematurely (eight months) in a macerated condition.

She now underwent varied but irregular antiluetic treatment with mercury, potassium iodide, and iodipin internally. Conception took place promptly, and one year after the first confinement she was delivered at full term of a macerated feetus. In view of this renewed evidence of latent disease, she submitted to a course of specific treatment by subcutaneous mercurial injections.

After an interval of some two years she conceived again, the last menstruation having begun October 20, 1902. She enjoyed apparent good health up to April, 1903, when she first complained of severe headaches. She was instructed to send her urine for examination, but, the headaches having left her in the mean time, she neglected to

do so.

Four weeks later she presented herself with a train of disturbances: nose-bleed, headache, vomiting, cough, dyspnæa, palpitation, diplopia, blurred vision, and impaired hearing. She passed but little urine and noticed that it foamed on passing (a sign of albuminous liquids noted, I think, by Hippocrates). Examination revealed the presence of considerable albumin. The excretion of urea was diminished. With the exception of slightly swollen eyelids, no cedema could at any time be discovered.

An ophthalmoscopic examination was made on June 1st by Dr. Schapringer, of this city, and his report stated the presence of

"retinitis albuminurica."

The patient was now kept in bed on a milk diet and treated with hot baths and antilnetic as well as eliminative medication. - No improvement followed, the condition becoming gradually but steadily worse. Muscular twitchings in the legs appeared from time to time, and, in addition to the uramic manifestations (headaches, vomiting, insomnia), a right-sided facial paralysis supervened. Under these threatening toxemic circumstances delay was fraught with danger, and the induction of premature labor was decided upon ex consilio. The patient was transferred to a private hospital and interference inaugurated on the morning of June 10th by packing the cervix with iodoform gauze. Slight pains appeared during the day and some bleeding took place—a welcome occurrence, in view of the high vascular tension. Twenty-four hours after the packing the cervix was sufficiently softened to permit rapid dilatation with the fingers under chloroform anæsthesia. The hand was now introduced, version performed, and the baby extracted without difficulty.

The puerperium ran an uneventful course, and on June 25th the patient returned home.

The child, a boy, weighing three pounds and five ounces, showed no signs of syphilis. He was tentatively placed in an incubator, but did not bear the latter well and had to be removed. Surrounded by hot-water bags, he lived two weeks.

Promptly following delivery a striking improvement became evident in the mother's condition. The vomiting, headaches, and a host of uramic complaints ceased at once. She remained sleepless for two nights, but afterward slept soundly. Her appetite returned. Vision, which had been so dimmed that she could not recognize a person at her bedside, began to clear up noticeably, and by the end of the first week she was able to read large print. She passed an abundance of urine which, three days after delivery, contained only a trace of albumin.

The improvement of vision was henceforth progressive. An ophthalmoscopic examination made on July 20th showed only traces of the former white deposits on the retina. Some astigmatism was also found. With correcting glasses vision soon became perfect.

The facial palsy participated in the general recovery. After two weeks the effaced folds reappeared, largely restoring to the face its lost expression. The eye could be completely closed in three weeks. Drinking was soon no longer difficult owing to escape of fluids from the corner of the mouth. By the sixth week nearly all traces of the palsy were gone.

Examined three weeks after delivery the urine still showed some albumin, and does so to this day. We shall come back to this fact

presently.

As will be granted, the case presents several noteworthy features. First, did the woman have syphilis? At no time were there any clear manifestations of the disease. This in itself is, however, no exceptional occurrence. Says Hutchinson: "Cases are innumerable in which a young wife remains in perfect health, never manifesting the slightest indication of disease, and yet bears an infant destined to show it." Such mothers, according to Colles' law, can suckle their syphilitic infants with impunity, while a healthy wet-nurse is in danger of infection. Some alleged exceptions to this law have been recorded and advanced in support of direct parental transmission with non-involvement of the mother. In the light of recent research,1 however, Colles-Baumès' law appears to be unexceptionally valid, and the mother of a congenitally syphilitic infant is without exception and permanently immune against syphilis, not only of her own child, but against infection from any source whatever. Now, such a lasting immunity can be acquired, as in other infectious diseases, only by passing through an actual attack, since inheritance is able to confer no more than a transitory immunity,

<sup>&</sup>lt;sup>1</sup> Rudolph Matzenauer. Wiener klinische Wochenschrift, February 12, 1903.

as plainly shown, for syphilis by authentic instances of sub partu infection (children infected with primary sores in passing through the genital tract of the mother). It would seem to follow, therefore, that every immune and apparently healthy mother has or has had latent syphilis. Such mothers not infrequently suffer at a later date from the tertiary manifestations, thus demonstrating a posteriori the correctness of the deduction. The important bearing of these considerations on prognosis and treatment is obvious. We may thus safely assume that our patient has passed through actual

syphilis.

This inference is not without bearing on the nature of the facial paralysis in our case. Could the palsy have been luetic in origin? It involved both upper and lower peripheral branches. There was greater involvement of the lower, however. The affected eye could not be closed voluntarily without closing the other eye, while simultaneously with the latter its closure could be partially effected. The unaffected eye could be closed singly. This "sign of the orbicularis" has been looked upon by Board as pathognomonic of central paralysis, though Jacoby has found it present in peripheral palsies, and therefore inconclusive. W. M. Bechterew quite recently has also observed the sign in peripheral facial palsies, but at a later stage, as a remnant of the affection. This illustrious author has demonstrated by experiments the value of the "orbicular sign" as pointing to a cortical or subcortical lesion. Winking in our patient was unaffected, both eyes participating in the act. Taste remained unimpaired.

In discussing the probable nature of the palsy, we must consider that slight hemorrhages into the retina and nose-bleed had occurred. Moreover, the time of appearance would rather lead to a non-specific explanation. The assumption seems to be most likely that a small central hemorrhage was responsible for the paralysis. Or, perhaps, the causative lesion was a localized cedema of the brain, as happens occasionally in uramia. Finally, the palsy may have been purely

toxic in character.

We now come to the most important aspect of our case, namely, the nature of the renal affection. Was it organic or was it functional? Did we deal with a genuine nephritis or with the so-called kidney

of pregnancy?2

The existence of a nephritis antedating the last pregnancy is rendered unlikely by the anamnestic facts: not only were none of the corresponding complaints present, but the urine had been repeatedly examined by the attending physician and nothing disquieting had been found. It is thus safe to assume that the renal disturbance originated in the last pregnancy.

The kidney of pregnancy, according to Leyden, consists in anæmia of the organ with fatty infiltration of the renal epithelium, but without inflammatory changes. Attempts have been made to

Obosrenie Psychiatrii, August, 1903.

account for this anemia by the vascular constriction consequent on reflex irritation from the pelvic organs, by direct pressure of the uterus, by mechanical retention of urine, etc. There is a growing tendency, however, to attribute the renal changes during pregnancy (together with certain changes in the liver) to the action of toxic metabolic products, the accumulated waste matter of maternal and fetal metabolism. That toxic substances are often the cause of renal lesions is sufficiently well established, and, reasoning by analogy, it is easily conceivable how in pregnancy the metabolic poisons may inflict an injury on the renal tissues. At first the impairment may be slight, but prolonged action or great intensity of the poison is likely to result in more serious damage, which may finally culminate in a true nephritis. It is quite plausible, furthermore, that the auxiliary factors mentioned above contribute their share to the result, for there is no doubt that the toxemia of pregnancy is a complex condition. The possible cumulative effect of repeated pregnancies may be a matter of etiological speculation, as may also in our case the antecedent syphilis and the mercurial injections.

With the removal of the causes the renal insufficiency of pregnancy would naturally tend to subside or disappear, as we actually observe in many such instances after delivery. When, however, the renal lesion has become more pronounced, it is perfectly comprehensible that it should persist after the primary cause has been removed. As a matter of fact, it has long been noted that genuine nephritis not infrequently becomes superimposed on the kidney of pregnancy. Even Leyden, who considers the renal disturbance as merely functional, holds this opinion. But here, as so often, no fixed line exists between functional and organic, the interval being filled up by intermediate transitional forms.

In our case the presence of such symptoms as retinitis and paralysis would point to a graver renal lesion and render the persistence of the

latter after delivery highly probable a priori.

This conclusion has, in fact, been borne out by subsequent observation of the patient. At the time of writing, six months after delivery, the albuminuria still persists, and the urine contains morphotic constituents indicative of renal involvement. Occasionally ædema of the eyelids is noted in the morning, and the woman complains at times of headaches, gastric distress, etc.

In view of this and the empirical observation that successive pregnancies cause more extensive retinal degeneration, future conception

in our patient will have to be prevented a tout prix.

# ON THE OCCURRENCE OF CYSTIC CHANGES IN THE MALPIGHIAN BODIES ASSOCIATED WITH ATROPHY OF THE GLOMERULUS IN CHRONIC INTERSTITIAL NEPHRITIS.

## By Edwin Beer, M.D., of New York.

(From Prof. Chiari's Pathologico-anatomical Institute in Prague.)

During the past few years the Malpighian bodies of the kidney have been studied in greatest detail, not only in normal but also in diseased organs. Of the pathological changes, those associated with fibroid atrophy in chronic nephritis have, perhaps, been most thoroughly investigated. There is no doubt that this latter form of degeneration and atrophy of the glomerulus is well recognized, even though there are diverging views as to all the changes that precede the formation of the hyalofibroid spherical mass.

In the literature very little mention is found of another very frequent form of atrophy within the Malpighian body in the same disease, chronic interstitial nephritis, and it is to the histological pictures of this, as well as its relative frequency, that I hope to call

attention in this paper.

In the literary synopsis which follows, it will be seen that the investigators of the early part of the second half of the last century, when thin sections and other refinements of technique were unknown, mentioned a cystic condition of the Malpighian bodies, whereas the recent writers ignore the condition. Rokitansky and Klebs, especially the latter, call attention to this in chronic inter-

stitial nephritis, describing one phase of the change.

In the Anatomie pathologique (1879) of Laboulbène and in the Histologie pathologique of Cornil and Ranvier, published in 1884, the cysts that are found in chronic interstitial nephritis are discussed at some length. The frequent occurrence of these and their origin from uriniferous tubules they affirm, but they also mention as a rarity (Cornil and Ranvier) cystic developments from the Malpighian bodies in which the capillaries have almost entirely disappeared, just a few remaining attached somewhere along the wall of the cyst.

In the 1893 edition of Orth's Special Pathology, a cystic atrophy of the tubuli and Malpighian bodies in contracted kidneys and chronic interstitial nephritis is mentioned, but in the 1900 edition-of his Patholog. Anat. Diagnostik he talks of these cysts as derived from tubules alone. Whether this is a change of view I do not know, but the fact that Baum, from Orth's laboratory, in 1900 published a paper in which he describes such a change in the Malpighian body as I am about to depict, and calls it a development anomaly or embryonic Malpighian body, suggests that in 1893

Orth's remarks were not intended to cover this peculiar pathological change, otherwise his pupil would have interpreted the picture in accordance with the earlier expressed views of Orth, or, at least, made some reference to the same.

In a picture in Dürck's Atlas of General Pathological Histology, p. 74, a cystic development from the Malpighian body is beautifully drawn. The lining membrane of the cyst is the typical wall of the Malpighian body—that is, Bowman's capsule—flat epithelium on a membrana propria; and at the right lower corner of the cyst are a few cells projecting into the lumen thereof, grouped irregularly about a bloodvessel. This cyst is filled with colloid, and is just the kind of cyst that is so commonly found in my researches. Dürck calls this a tubulus cyst. Otherwise little or no mention is found in reference to this change, except, perhaps, in Philippson's article (also in that of Beckmann), in which the former says he found hydrops of the Malpighian bodies similar to that seen in so-called congenital cystic kidney in kidneys of older people, but specifically states that there seems to be no relation between this and chronic interstitial nephritis (p. 556).

On the other hand, in Israel's (1889), Weichselbaum's (1892), Hamilton's (1894), Orth's (Diagnostik, 1900), Ribbert's (1901), Schmaus' (1901), Kaufmann's (1901), Ziegler's (1901), Langerhan's (1902), and Dürck's (1903) text-books the fibroid changes in the Malpighian bodies are discussed in more or less detail, but no mention of another—i. c., cystic atrophy—is made. Weichselbaum, to be absolutely accurate, suggests such a possibility, while Ziegler and Ribbert mention the calcification in Malpighian body cysts

that were described by Baum.

To avoid any mistake, I must mention here that the not uncommon macroscopic cysts lined with cuboidal epithelium, containing variously colored fluids and fluids of various consistency in chronic interstitial nephritis, are quite different from those to which I am about to call attention. These tubule cysts are very commonly visible to the naked eye, whereas the form that is derived from the Malpighian bodies is only occasionally so recognizable. If these latter are large enough to be seen by the naked eye, the microscopic examination alone can distinguish them from tubule cysts. Moreover, what I am describing has nothing to do with the small cysts that have been found in glomeruli that are undergoing the fibro-hyaline atrophy. These "cysts" are minute spaces made by the irregular growth of tissue within Bowman's capsule and scarcely deserve the name cyst. They involve a small part of the whole Malpighian body and are only an indication of irregularity in growth of the newly forming intracapsular tissue (Engel, Tschistowitch).

Here it must also be mentioned that the cysts that I am calling attention to have been interpreted as tubule cysts by some authors

—e.g., Dürck—as seen in the illustration referred to previously. Orth and Baum have expressed somewhat similar views, while Cornil and Ranvier talk of most of these same cysts as tubule cysts in which the epithelium has been flattened out. In single sections, where remnants of the glomerulus are usually not seen projecting into these cysts, this view of their origin might seem justifiable. It is probably due to this misinterpretation that we find so little mention of a second form of atrophy of the glomerular structures in medical literature.

From the foregoing it will be seen that more or less complete descriptions of four different kinds of cysts derived from the kidney parenchyma in chronic interstitial nephritis are found in the literature. Two are referred to the Malpighian bodies and two to the tubules. Of the former, one is scarcely a cyst, while the other, of which very little mention is found in the literature, deserves that appellation, but has never been studied and clearly described.

Of the so-called tubule cysts, the two varieties differ most markedly, according to Cornil and Ranvier, Orth, and Baum, not to mention others, in the nature of their epithelium; in one these cells are more or less high and cuboidal, whereas in the other they are completely

flattened out against a membrana propria.

The studies that underlie this article are based on twelve kidneys of chronic interstitial nephritis which were examined in serial section and thirty kidneys in single section (i. e., non-serially), to determine both the origin and the development of the cyst in question and also the frequency of their occurrence. The serial sections demonstrated the origin of a large number of cysts, those with "flattened epithelium," from the Malpighian bodies, by showing atrophic glomerular structures adhering to the wall of the cysts, and the study of the single sections from the thirty kidneys with chronic interstitial nephritis showed that cystic atrophy is a very common occurrence.

In the usual non-serial sections of kidneys in which chronic interstitial nephritis is found, one sees cystic spaces filled with a more or less homogeneous substance. The walls surrounding this substance are made up of two elements, a basement membrane and a layer of epithelial cells attached to it. In some of these the epithelium is flat, so that only here and there a nucleus, with a small amount of flattened protoplasm surrounding it, is visible; while in others, again, the epithelium is arranged as in the uriniferous tubules, the nuclei being near one another and the cells to which they belong being more or less cuboidal in shape. These two kinds of cysts impress one as very different structures. The wall of the former is identical in structure with that of the Malpighian bodies— Bowman's capsule—while the wall of the latter reminds one of the uriniferous tubules. In addition to these cysts, one occasionally sees an altogether different picture. One finds a cystic formation and projecting into the contents of the cyst (Figs. 1 and 2) are tufts

of capillaries, distinctly part of the glomerular tufts, but smaller in size than the normal capillary mass. The walls of these cysts are identical in structure with the walls of a normal Malpighian body, and, moreover, absolutely identical with the walls of the first of the above-described cysts—i.e., flattened epithelium—whose nuclei are far apart (in usual sections), lying on a basement membrane.<sup>1</sup>

The size and general contour of these two "varieties" of cysts with walls of identical structure vary very much. In general, they are a little larger than the normal Malpighian bodies and more or less spherical. At times they are five to six times (in one plane) the size of the Malpighian bodies; at others even larger. They may be very irregular in shape, sending prolongations in between the tubules.

Of these two "varieties" the second is undoubtedly that to which Laboulbène, Cornil and Ranvier, and Baum refer, while the first is usually interpreted as a tubule cyst, despite the resemblance its walls bear to the normal Bowman's capsule and to the capsule of

the cysts with small capillary glomerular tufts.

If these cysts that have been interpreted as tubule cysts with flattened epithelium are cut in serial section, in the majority of cases, one finds that at some spot attached to the wall and projecting into the lumen arc some remnants of a glomerulus, very often one or more capillary vessels. In other words, those cysts with walls that resemble in their structure the walls of Malpighian bodies contain an atrophic glomerulus, so that in one or more sections one gets a picture such as the above authors have mentioned, while in all theother sections one gets the "variety" which has been interpreted as a tubule cyst with much flattened epithelium.

Having thus made clear the point that these eysts, so-ealled tubule eysts, are derived from the Malpighian bodies, I shall briefly point out the stages in this form of atrophy of the glomerulus, noting how both the capillaries and the visceral layer of Bowman's capsule

behave in this process.

From a study of a great many sections in series, one can describe the various stages in this atrophy by a connected statement better than by describing in detail selected pictures. This I shall attempt in the following pages, repeating as little of what has been mentioned.

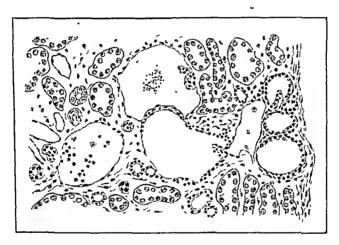
as accuracy will permit.

These eysts derived from the Malpiglian bodies are, perhaps, most frequently found in the superficial cortical part of the kidney, and they vary, as just said, very much, both in their size and shape. They may be only slightly larger than a normal Malpiglian body, but at times they are much larger and even visible to the naked eye. Their shape is most usually almost spherical, but it is not uncommon to find them very irregular in outline.

As seen later other cysts of Malpighian origin show different remnants of the atrophying glomerular tufts, which are, however, rarely noted in non-serial sections.

The walls of the eysts are made up of flat epithelium lying on a basement membrane, absolutely identical with the structure of the normal Bowman's capsule. In serial section one finds any stage of atrophy between a fairly normal-looking eapillary mass, smaller than the normal vascular tufts projecting into the cavity, to a single eapillary vessel just projecting into the eavity of the eyst. At times not even this is seen, as detailed below. In the usual non-serial diagnostic section one more often finds no sign of the glomerulus, but occasionally, as in one of my specimens, one can see several cysts close together in one field (Fig. 1), in several of which one or two capillaries are visible. One can understand the whole process by finding these various stages in this atrophy of the capillaries from the cysts with fairly normal-looking capillary tufts of nearly normal size to those with only one or two vessels.

FIG. 1.



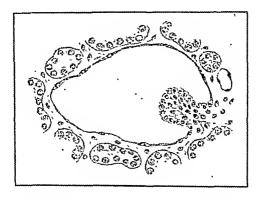
Shows directly under the kidncy capsule three dilated tubules, and lying above these four Malpighian body cysts. Two of these show remnants of the glomerulus, the other two in this section show none. In two of the cysts, cells lie in the "colloid," in one fine granules of lime, and the fourth contains only the "colloid," (Drawn with 2 A. Zeiss.)

Rarer than these forms, of which the cyst with only a few vessels is the one most commonly seen in my serial sections, are those cysts that show no signs of glomerular vessels at all. Probably the relative frequency of one or the other stage of the atrophy in the glomerulus is dependent on the severity of the interstitial nephritis.

Not infrequently the visceral layer of Bowman's capsule, which now is fairly generally looked upon as a syneytium (Kölliker-Ebner), behaves in a very interesting way, which shows that the eells still retain individual characteristics, even if the theory of their syncytial life under normal conditions is true. In some of these Malpighian cysts in which the glomerular tufts are quite small, consisting of just a few capillaries, this visceral epithelial layer is very prominent, and

each cell is distinctly visible (Fig. 4), their outline being definite and clearly distinguishable. In other cysts, though the nuclei stand out close together, as in the fetal kidney, the cell limits are indistinct (Fig. 3). Moreover, many of these cysts, where little or nothing of

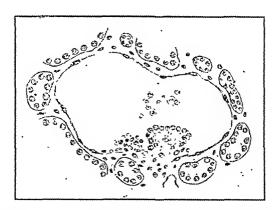
Fig. 2.



Shows similar cyst, but in this the cells of the syncytium have become individualized, each one being distinctly separable from its neighbors.

the capillaries remain, show small papillary excrescences covered with epithelium (Fig. 3), which, from their anatomy and the analogy they bear to other cysts, must be interpreted as a remnant of the syncytium supported on a tender branching framework of what

Fig. 3.

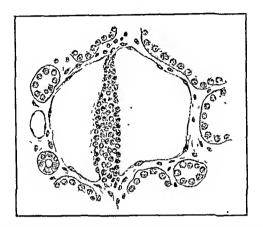


Shows similar cyst, in which the visceral layer of Bowman's capsule has become very prominent.

seems to be connective tissue. At times this more or less branched structure is attached to the cyst wall at both ends, dividing the cyst in some sections into two smaller cavities, which, however, communicate in the following sections of the series (Fig. 6).

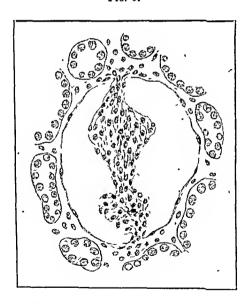
The origin of this dividing, incomplete septum or bridge is seen in the following process: occasionally the glomerular tufts (Fig. 5) become attached to the parietal portion of Bowman's capsule, more

FIG. 4.



Shows similar cyst, but here the capillaries have disappeared, and the proliferated visceral layer of Bowman's capsule has covered the bridge with epithelium.

Fig. 5.

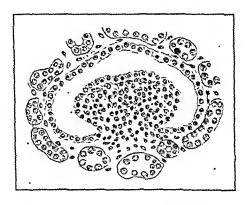


Shows another cyst in which the capillaries have become adherent opposite to the hilus. Pressure lines are distinctly visible running parallel from the hilus to the capsular adhesion.

or less opposite to the entrance of the artery of the glomerulus. The capillaries gradually undergo atrophy, so that in some pictures one can see a few capillaries running through the central part of the cyst, dividing it into seemingly two smaller cavities. With the

proliferation of the visceral layer of the capsule, when the capillary atrophy becomes extreme, a mass of epithelial cells, on a connective-tissue framework, is found running through the cyst, dividing it into two more or less equal parts (Fig. 6). Whether these papillary bodies and the rejuvenescence and proliferation of the epithelium of the visceral layer of Bowman's capsule, that were just described, have anything to do with the production of kidney tumors, I am not in a position to state definitely. That such a possibility exists cannot be denied, and further investigation must determine the relation between these processes and those that lead to tumor—e.g., adenomata formation. In this connection, it is of interest to note that Grawitz, in his criticism of the work of Weichselbaum and Greenish, who referred the latter structures—i.e., adenomata—to the epithelium of the uriniferous tubules, said that he had seen pictures which suggested a Malpighian origin. Ricker saw a similar

Fig. 6.



Shows a dilated tubule into which the growing connective tissue has pushed part of its wall, thus mimicking a Malpighian body cyst.

picture in an adrenal, "rest," which he interpreted as a papillary growth. In view of these facts, and also in view of the fact that adenomata are not uncommon in chronic interstitial nephritis, this peculiar change that I have described in some of the Malpighian bodies that are undergoing the cystic atrophy must be kept in mind, and, perhaps, it will aid us in interpreting some of the new-growths of the kidney.

In all the cysts already described there is found some remnant of the glomerulus, but, in addition, one finds cysts of identical structure without any sign of the glomerulus projecting into their cavities. In these cysts the contents and the walls are of absolutely the same nature as those cysts which still show capillaries or the visceral layer of Bowman's capsule; and in single section the cysts that contain atrophic elements of the glomerulus and those that do not cannot be distinguished one from the other, unless the section happily strikes

the plane of the atrophying glomerular structures in the former variety of cysts. Even then only serial section will make sure that no glomerular elements persist in the second variety of the above cysts. This absolute identity in structure between the cysts that contain glomerular elements and those that do not leave no doubt as to their common origin from the Malpighian body. The absence of all glomerular elements may be the final stage in the atrophy of the glomerulus.

That this process of cystic atrophy does not seem to be due to inflammation within the Malpighian bodies must be emphasized. No signs of inflammation either in the capillary tufts nor in the parietal layer of Bowman's capsule were ever seen, except, perhaps, in that form of atrophy in which the capillaries had become adherent opposite to the hilus. No marked signs of inflammation between capillaries and Bowman's capsule were seen even here, but the adhesion probably owed its origin to some such process. All the other pictures—the usual ones—point rather to a mechanical factor without the Malpighian body as the direct cause of this condition

of cystic atrophy.

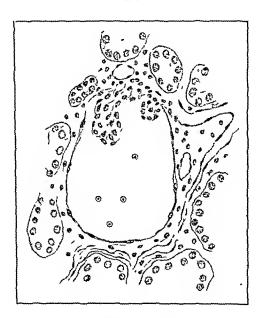
The contents of these cysts vary very much. The ground substance, if I may use that term, which fills them usually takes varying deep tints with eosin, stains yellow with Van Gieson, very faintly with hæmatoxylin, and similarly with alum coclineal, but still fainter after treatment with acids; in general, it has the characteristics of what is called "colloid." In this "colloid," which shrinks in hardening, leaving a more or less irregular space between it and the cyst walls, there are quite often various cells-leukocytes and epithelial—also not infrequently lime-salts, as I have described in another recent article in the Journal of Pathology and Bacteriology. It must be mentioned that in some of these cysts the fluid does not stain, but such cysts are quite rare and unusual in my experience. No indication of a direct change of the capillary tufts into this "colloid" were ever noticed, so that this, in all probability, is a product of secretion rather than a degeneration of previously normal protoplasm.

In looking for a tubulus contortus in connection with these cysts, it was the rule not to find any. Practically all of the cysts were blind, and this probably helps to explain their origin. Somewhat similar cystic Malpighian bodies are seen in congenital cystic kidneys without the "colloid" contents, and from the similarity in the picture and the fact that the tubuli contorti seem to be usually shut off, I think we can assume that the Malpighian body cysts in chronic interstitial nephritis owe their origin to a similar mechanical process, to obstruction in the efferent uriniferous tubule. Whether the very few cysts into which a tubulus contortus could be traced owed their origin to an obliteration or stenosis of this tubule some short distance from the Malpighian body, instead of directly at its origin from this

body, I cannot state definitely. Perhaps, even in these there was a stricture at the insertion of the tubule into Bowman's capsule. It is of importance to note that where I found a tubulus contortus opening into a cystic Malpighian body, which in all my specimens I saw only a few times, the Malpighian body cyst was about the size of a normal Malpighian body.

What the nature of the process that leads to obstruction in the tubule is we can only guess at for the present, as it is almost impossible to imagine a method of investigating a stenosis of these channels. One would naturally think of the new connective tissue and its subsequent contraction, which is so characteristic of this form of nephritis, as the cause. It is of importance to state that I did not

Fig. 7



Shows Malpighian cyst with atrophic glomerulus flattened more or less against the cyst wall. Capillaries are still present. Contents of this cyst, cells and "colloid." (Figs. 2 to 7 drawn with 2D. Zeiss)

find any irregularity in the presence of new connective tissue about or near the cysts, but it seems likely that contracting bands at some distance might lead to occlusion of the tubuli contorti without being necessarily in absolute proximity to those tubules. Another method of closure might be within the tubule itself, as mentioned above, due to stricture formation. Perhaps future investigation will make these points clear.

Before leaving this general description I must state that although the signs of increased pressure within the Malpighian bodies were present in many instances they were scarcely the rule. In some cysts the remnants of the capillaries were spread out along one side of the wall, as if pressed and flattened there (Fig. 2). In the cases where adhesions had formed between capillaries and parietal layer of Bowman's capsule opposite to the hilus, the signs of pressure were even more distinct (Fig. 5); and the capillaries ran almost parallel to each other, being pressed together from the sides. The increase in size of the Malpighian bodies undergoing this cystic change and the frequent cystic prolongations between the tubules are also indications of a heightened pressure, as no signs of active proliferation of the capsule were visible in any case. That the increase of internal pressure must be very gradual in these closed-off Malpighian bodies is evidenced by the fact that most of the glomeruli undergoing this atrophy show no signs of active pressure in their general conformation.

From all the above it will be seen that in chronic interstitial nephritis the Malpighian body undergoes a change which is quite the opposite of the usually described "fibrohyalinization." This latter change most often depends on a vascular disturbance and leads to shrinkage of the whole structure, while the former, the cystic atrophy or degeneration, probably depends on a disturbance in the efferent uriniferous tubules, and leads to the formation of a cyst somewhat or much larger than the original Malpighian body. Both have in common the more or less complete destruction of the

glomerulus.

As to the frequency of occurrence of cystic atrophy of the Malpighian bodies, the following table, based on sections from thirty different cases of chronic interstitial nephritis, will show. In each case one section was gone over and both fibroid and cystic Malpighian bodies were counted and arranged in parallel columns:

THIRTY CASES OF CHRONIC INTERSTITIAL NEPHRITIS WITH ENUMERATION OF GLOMERULAR CHANGES.

Cases	š.				ystic rophy	Fibrohyaline atrophy.	Cases	š.					stic roph;	
1	•				8	3	19						1	3
2					3	2	20						2	0
3					10	7	21						0	2 -
4					4	3	22						0	5
5					0	2	23						1	0
6					3	4	24						0	2
7				area	0	81	25						2	3
	l in	non-	infai	cted	4	1	26						6	0
8					2	1	27						3	3
9	•	٠.			4	1	28						1	3
10		•			0	2	29						2	2
11	•		•		2	1	30						3	4
12	٠	•			1	1						_		
13	4				8	8			m. 1	. 1.				
14	٠	•			0	9			Tota	-	•	•	79	169
15	•		•		4	0	Exclusive of infarcted							
16	•				2	2	8	rea					0	81
17	•				1	13						_	_	
18	•	•		•	2	1 İ							79	88

It will be seen that these two changes are almost equally frequently seen if we exclude the areas where infarcts appeared in the sections, for here the vascular change was the direct cause in the overproduction of the fibroid atrophy. But even if all these areas are included in our estimate, the proportion of cystic to fibroid changes is surely a large one and well deserving of more attention than it has received.

Looking a little more closely at these figures, it is evident that in these thirty single sections 24S atrophic Malpighian bodies were found. Of this total 79 were cystic and 169 were changed into the well-known fibrohyaline masses. Expressed in percentages, 31 per cent. were cystically changed, whereas the rest had undergone fibrous atrophy. If those sections in which no infarcts were noted were considered alone the percentage of cystic to fibrous would be considerably changed. From this point of view, 47 per cent. would be cystic and 53 per cent. fibrous atrophy.

It is also evident that in some sections no representatives of one of the two pathological changes may be found, and in other sections one form is more frequently seen than the other. A similar table could be made from the kidneys that were cut in serial section, and this emphasizes the fact that the above enumeration from single

sections is absolutely reliable.

In closing, I wish to emphasize the two most important facts that have been brought out in the preceding pages:

1. In addition to the well-known fibroid atrophy of the Malpighian body in chronic interstitial nephritis there is also a cystic atrophy.

2. Cystic atrophy is very common and in my cases almost as fre-

quently seen as the fibroid change.

In closing, I wish to thank Professor Chiari for the material on which this work is based and for his many kindnesses while studying in his laboratory.

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## A PARTIAL STUDY OF ULCERATIVE ENDOCARDITIS.

# By Beverley Robinson, M.D., of New York.

THE subject of ulcerative endocarditis formed the thesis of Dr. Osler's Goulstonian Lectures in 1885. He begins them as follows:

"It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future." 1

It is with this spirit I have undertaken a renewed study of ulcerative endocarditis.

In 1898 Sir Douglas Powell delivered before the Royal College of Physicians of London "Lectures on the Principles which Govern Treatment in Diseases and Disorders of the Heart." <sup>2</sup>

In this third lecture he carefully considered those which specially dominate the treatment of ulcerative endocarditis. There he also reviewed the therapeutic measures likely to be of some use in the disease. He likewise gave a tabulated statement of the results of treatment by antistreptococcic serum, and of his own experience with yeast and with nuclein, after the method of Dr. V. C. Vaughn, of Michigan. In the Lumleian Lectures during the current year, Dr. T. R. Glynn<sup>3</sup> has again reviewed this subject and regarded it "mainly in its clinical aspects." He was influenced to do so because of its great clinical interest, and the fact that no disease presents itself under a greater variety and perplexity of forms. A very elaborate historic retrospect of our growing knowledge pertaining to the disease is at first dwelt upon. In it he cites Matthew Bailey, Morgagni, Senac, Corvisart, and Bouillaud. To the latter he ascribes the honor of associating ulceration of the cardiac valves with symptoms of typhoid fever. He shows how the "third period" was marked by a perfected bacteriological technique, and by the fuller comprehension of the biological characteristics of bacteria. Thus ulcerative endocarditis, which was formerly considered as a local affection, is now regarded as one of the complications of a general infection.

This malady, like the simple form of endocarditis, affects the lining membrane of the heart and especially the nerves. It is characterized by vegetations and is accompanied with loss of tissue. The ulceration may cause perforation of heart valves, or even of the septum or heart walls, under very exceptional conditions. With the ulceration we may find a limited area of suppuration. It is very rarely a primary affection, but ordinarily occurs as a

complication of some infective disorder, or septic disease. No doubt this view explains how it is that the lesions of simple endocarditis often precede and are found in conjunction with those of the more advanced or far graver form of the disease. Between the latter and the benign malady there is, indeed, no essential anatomical difference, and they merely represent gradations, as it were, of more or less intensity.

Although cases which have developed primarily are occasionally observed, they are so infrequent as to have had legitimate doubt thrown on them. Osler reports one case in which at the autopsy no lesions were found other than those of ulcerative endocarditis. In cases of obscure origin it is probable that the micro-organisms frequently enter the economy by the respiratory passages, and reach the heart in this way rather than through the digestive organs. Especially in cases of chronic heart trouble by reason of secondary congestion of the air-passages, the conditions become favorable to bacterial invasion. An infective endocarditis originating in this way would occasionally appear to be of primary origin. (Glynn.)

On the other hand, ulcerative endocarditis occurs quite frequently as a complication of pneumonia. "In 16 cases of 100 autopsies in which this lesion was present, 11 were of this form." According to Wells, the proportion in all cases of pneumonia is 3 per cent., while the percentage in fatal cases of the latter disease is 4 per cent. G. Studa's estimate of the relative frequency of ulcerative endocarditis in pneumonia is a much higher one (9 cases in 85 autopsies). When it is found in this disease it appears to be exceptionally virulent, as numerous autopsies demonstrate. It is also seen in acute rheumatism. Anders writes that the proportion is about 10 per cent. of the cases in which acute endocarditis appears. It may also occur as a complication of some emptive fevers and in septicæmia. Vaccination has been followed by cellulitis and infective endocarditis. (Coleman.)

Cases are likewise due to dental caries and oral sepsis. When we consider the great number of cases of acute and subacute rheumatism we are called to treat, the number of those complicated with

ulcerative endocarditis seems very small.

Ulcerative endocarditis often follows septicæmia of various origin, and is not uncommon in gonorrhæa. The intimate relations between some cases of gonorrhæa and ulcerative endocarditis have been established for more than twenty years, but it is only lately that these instances have been studied in a systematic manner. A fatal case of this kind has been reported. In some of these cases it has been impossible from the most careful local researches to discover the site of entrance of the infective disease. We should then turn to cultures made from the blood, and occasionally bacteria with the typical characteristics of gonococci will be shown. 10

The cultivation should be made during life, and it may be con-

firmed at the autopsy from blood taken from the heart, or from the cardiac vegetations. For the cultivation it is not essential to take a great deal of blood, to dilute it much, or to make use of special media. It is now known, also, that the bactericidal action of the blood is less pronounced on gonococci than it is on pneumococci or the typhoid bacillus. The septic process that proceeds from the puerperal state is also a well-known source of grave ulcerative endocarditis. Although certain authors have described it as a complication of malaria, it is questionable whether such cases often occur. Among diseases which are occasionally complicated with malignant endocarditis I would cite measles, scarlatina, small-pox, erysipelas, and typhoid fever. In my experience such instances, with the exception of the latter disease, have not been seen, and even of this finding I have no available record.

Cerebral complications are associated with it at times, particularly, as meningitis, and this is especially true when the malignant endocarditis is found with pneumonia. I have observed one case of obscure mental disorder in which the malignant endocarditis was shown to be "mural" at the autopsy, and no gross changes had taken place in the brain. Miliary abscesses have been found, however, in a number of instances. Once Jackson found an embolus of the artery of the Sylvian fossa, and Lartigau<sup>13</sup> reports a case of gonor-rhœal origin, in which prior to death there was a sudden aphasic attack. The bacillus of influenza has also been detected in the valvular vegetations of ulcerative endocarditis. The cases observed were instances of the development of the disease upon a chronic cardiac affection.<sup>14</sup>

This fact is important as pointing to a demonstration of what has long been considered probable, namely, the vulnerability of the heart to the influenza poison. Ulcerative endocarditis occurred in 4 of de Batz's 20 cases, and a most interesting example has been recorded by Tickell. It has been observed during the influenzal attack, but most frequently in the convalescing period.<sup>15</sup>

A new organism of endocarditis, called micrococcus zymogenes, has lately been pointed out in a patient who died. The infarcts which accompanied this case are not stated to be other than bland; therefore it may be that the endocarditis itself belonged to the simple type. On the other hand, Maccullum and Hastings report a case caused by this organism, in which multiple septic infarctions in various viscera were found. Further, typical acute vegetative endocarditis was experimentally produced by intravenous inoculation in a rabbit and a dog, and the cocci were demonstrated in pure culture in the vegetations and in other parts of these animals after death. The micrococcus zymogenes is stated to be extremely minute, often elliptic in outline, usually found in pairs, is not motile, and stains with the ordinary stains.<sup>16</sup>

Although it is stated by some writers that the two forms of the

disease, simple and ulcerative, never become one and the same, this affirmation is probably too positive. Litten believes that prompt response to the salicylates is characteristic of the benign form.17 They may be used, therefore, with some measure of reliance to determine an otherwise doubtful diagnosis. Litten also criticises Lenhartz's views as to the fact that the finding of micro-organisms in the blood characterizes the endocarditis as septic. Very justly he remarks that if later the microbe of acute rheumatism be accurately determined, such distinction will be no basis to rest upon. In the septic-malignant form of Litten, suppuration occurs in thrombi and joints, which does not occur in the non-septic malignant form. He objects strongly to the term "ulcerative" endocarditis, but does not believe the time has come to make separations on the ground of the presence or differences of micro-organisms. Poynton and Paine consider that ulcerative and other forms are only different degrees of the same disease, and that benign forms may become malignant under the "influence of virulent breeds" of the common micro-organism of rheumatism. Ewart insists that, even though the practical identity of the organisms may not be proven, a very important clinical lesson is furnished. This essentially means that our efforts of prophylaxis in rheumatism should be strengthened, because in prophylaxis of this disease we also combat the development of most serious cardiac affections.18 An equally important matter has already been insisted upon by Sir Douglas Powell in his Lumleian Lectures where he directs "attention to the necessity of observing certain prophylactic precautions during convalescence in rheumatic endocarditis" (loc. cit., p. 1153). The lesions found may be in the heart, or other organs of the economy.

In Jackson's cases enlargement of the spleen was present in all but one instance. Leukocytosis was also regularly found, the leukocytes usually numbering from 16,000 to 20,000. This is an important point in the differential diagnosis from malaria, tuberculosis, and typhoid fever. The bacteria in the blood are important and have different forms. In 23 cases studied bacteriologically by Jackson "in 2 no cultures were obtained; in 2 there were microorganisms which were not identified; in 8 streptococcus pyogenes was found; in 5, the pneumococcus; in 3, staphylococcus aureus; in 1, the colon bacillus; in 1, the streptococcus and staphylococcus;

and in 1, the streptococcus with other organisms."

In the 38 cases discussed by Lenhartz, the author carried out bacteriological investigations in 28 cases. In 16 cases bacteria were found during life. They were principally staphylococci. According to Lenhartz it is usually comparatively easy to find the organism in the blood. From the point of view of prognosis it is very desirable to differentiate between the various forms of ulcerative endocarditis. This may be accomplished by careful blood cultures during life. It is especially desirable at present, by reason of the more

hopeful outlook of these cases. This seems to be proven partly by the results from treatment, partly by the data afforded by careful autopsies. Ewart, indeed, has stated, even in cases that resulted fatally, that evidences of repair in the local cardiac lesions could be shown. It may be remarked that there is little tendency in this process toward cicatrization, so that recovery may take place with little or no deformity of valves or orifices. (Wells.) The cardiac changes will depend upon the nature of the organisms which occasion them, and also upon the extent and duration of the disease. We do not find the same conditions in instances in which the process is wholly acute, and those where the acute disease is attached to former sclerotic changes of the valves. Usually we find vegetations on the valves. These are often found with an ulcerative process and small abscesses. According to Wells the distinguishing features of them are their massive character and broad base. Moreover, they do not extend often beyond the valves. The left heart is more frequently the site of the disease than the right. In regard to this point errors may be found in literature. Still the right heart is

attacked oftener than in the benign form.

Mural ulcerative endocarditis is extremely rare. I have seen only one case, to which I have referred. The history of another one, . hitherto unpublished, has been kindly given to me by my colleague, Dr. Van Horne Norrie. In rare instances the process may extend to the aorta and pulmonary artery. A secondary infective arteritis in various peripheral situations and in the different viscera, as a result of septic embolism from the heart, may also occur.20 The vegetations are frequently small, especially when they alone are present. They are of gray or yellow color, and are situated on the margin or at the base of the valves. Under the microscope they are shown to be composed of numerous microbes, embryonic cells, and leukocytes. They also contain fibrin.21 In many instances, however, the vegetations are larger and may become pedunculated. They have a markedly gray aspect also, or are covered with blood clot, and often show superficial or deep ulceration of tissue. In the latter case an aneurysmal pouch may be found. This pouch formation doubtless is due to blood pressure upon softened and degenerated valvular tissues. Sometimes the ulceration goes deep enough to make a perforation of the valve. Again, it extends to the chordæ tendineæ, beginning in the inflammatory stage, and separates later the valve segment completely. When this takes place we may have a flapping with each ventricular contraction of the detached valve against the auricle. Thus, secondary infection of the auricular walls is produced, and it is not uncommon to find warty growths here situated. In rare instances when the ulceration has enlarged and become still deeper, the septum or ventricular walls may be perforated. If the malignant endocarditis be caused by pyogenetic organisms it is not uncommon to find small abscesses in the valves,

or, indeed, in other parts of the heart. These abscesses may rupture, sometimes with perforation of the heart walls, and then pus is found in the pericardial sac. It is also possible for small quantities of pus to be reabsorbed, and the evidence of this is found in old scar tissue, or calcareous deposits. In some cases, especially when malignant endocarditis is found in a patient suffering from chronic heart disease, the vegetations may be capped with calcareous incrustations. In very rare instances the deposit of lime salts may occur in acute cases.

The ulcerative condition of malignant endocarditis may possibly be confounded with that which follows the necrosis of former atheromatous deposits, or those incident to chronic rheumatic endocarditis of benign nature. A differential diagnosis may here be made, probably with the use of the microscope; but at times doubt may still remain. Osler, in an analysis of 209 cases, showed the proportion in which the different valves, the walls, and sides of the heart arc involved. His report reads "aortic and mitral valves together, 41; aortic valves alone, 53; mitral valves alone, 77; tricuspid in 19; pulmonary valves in 15, and the heart wall in 33 instances. In 9 instances the right heart alone was involved; in most cases, the auriculoventricular valves." 22 In Strada's 85 autopsies the seat of the affection was in the left side of the heart alone in 6 cases, and in the right alone in 3 cases. In Jackson's 43 examinations post-mortem we find that "the aortic valves were affected in 9 instances; the mitral, in 15; both, in 10. The right side of the heart was involved 6 times, and the endocardium of the ventricle 3 times. In 5 of the aortic cases there was old endocarditis; it was present in 7 of the mitral cases. The malignant disease had become implanted upon the old disease."

The mechanical factor, however, is not considered essential by Lenhartz, and he has shown that fresh endocarditis does not always arise at the site of the old endocarditis if the latter is present. In Glynn's cases "the infective endocardial lesions were distributed as follows: the aortic and mitral valves were involved in 21 cases, the aortic in 10, the mitral in 15, and the endocardium of the ventricle alone in 1. The right side of the heart was involved in 6 instances" (loc. cit., p. 1073.) Mural endocarditis is apt to affect either the upper portion of the septum of the left ventricle or the

posterior wall of the left auricle.

According to the analysis of Kantback and Tickell, in 84 cases there were 51 males and 33 females; and in all but 16 cases old cardiac lesions were found. (Allbutt, p. 877.<sup>23</sup>) In Glynn's cases he found 65 per cent. of patients were males and 34 per cent. were females—"figures approximating those of Dr. Osler." The disease occurred, however, more frequently in young women than in young men. It was also remarked that the disease was likely to occur under conditions attended with general debility. In only

7 per cent. of the cases had an inflammation of the lungs preceded the endocarditis; in 11 per cent. of his cases the endocarditis originated in a recognized infective focus. The vegetations may become detached in larger or smaller masses and, carried by the circulation, form embolic plugs in different organs. Notably we find the kidneys and spleen affected; less frequently the brain and intestines are involved. The place where the embolic mass is arrested depends largely upon its size. While small emboli are more apt to be seen, it is not unknown to have a large artery completely obstructed. If the lungs contain infarcts, the embolic plugs originated in malignant endocarditis affecting the right heart. The embolic plugs are more or less numerous. In some cases where the malignant endocarditis is very pronounced and the ulcerative condition extensive, the autopsy does not show any embolic processes in the organs. They are also more or less irritating.

Consequent upon the degree of their infective nature follows the rapidity with which abscesses are formed. At the site of these abscesses it is not uncommon to find the arterial vessel already softened and ulcerated. Very many small abscesses are found at times in different organs of the body. Sometimes hemorrhage may be combined with the abscesses. Why in some cases the one is more frequent than the other is not positively known. (Strümpell, Practice of Medicine, 1901, p. 306.) Embolism was found to be "nearly three times as frequent in the infective as in the simple cases." (Glynn, p. 1076.) It is noted, contrary to the usually accepted opinion, that the so-called infarcts are not due to embolism, but are the result of "apoplexies" following the rupture of small bloodvessels, and made "specially liable to occur in severe passive

congestion of the lungs."

The micro-organisms found in malignant endocarditis are pneumococci, streptococci, staphylococcus pyogenes aureus and albus, the gonococcus, and other organisms. The former are most frequently concerned, either alone or associated with others. The pneumococcus infection is more frequent in aortic endocarditis, the streptococcus infection in mitral endocarditis.24 septic diseases malignant endocarditis is prone to occur, there are cases in which the valves are but slightly involved. In no case does the endocarditis form more than a part of the general septic condition. If, however, the heart is notably affected, it hastens very much the spread of the poison, and thus this organ becomes very important in the estimate of the gravity of the case. Of course, there is in these cases the local disease of which the malignant endocarditis is the result. This may be of the nature of an acute necrosis, a wound abscess, or puerperal disease, when there may be primary septic foci in the uterus, or its adnexa.

The etiology of the disease is varied. This is known. Many cases follow an infectious disease, especially pneumonia. This fact

has been pointed out by Osler. Still there are cases which appear to be primary (Jackson), as no assignable or sufficient cause of their development can be discovered. All forms of endocarditis, whether ulcerative or benign, seem, according to later investigations, to be of parasitic origin. This view had been entertained also by Bartel. According to this anthor, in cases of rhenmatic origin the organisms soon die, and often are not discoverable, particularly in cases which have run a somewhat chronic course. There are, however, some cases which "are apparently not due to the direct action of micro-organisms." These are caused by thrombotic deposits, and are possibly the results of the action of bacterial toxins.†

In a peculiar case of endocarditis reported by Hopkins and Weir, in which death resulted from cerebral hemorrhage, we have one that "seems to belong to the group on the border-land between a septic and alcerative endocarditis; all the emboli were simple, not

septic."

Thayer and Lazear<sup>25</sup> have gone thoroughly into the subject of gonorrhœa as a cause of septicæmia and ulcerative endocarditis. In their paper they show that the discovery of the gonococci in the circulating blood and upon the cardiac vegetations was made by Blum in 1895. The endocardium may be directly attacked by the gonococcus, as the general infection may be the immediate cause of the local trouble.

Ulcerative endocarditis is a rare disease in childhood. When it does occur in childhood it does not differ essentially from the disease in the adult. One case is reported in an infant ten months old, by L. D'Astros,26 which resulted fatally. This case followed diphtheria, and, as was shown at the autopsy, was the result of a staphylococcus infection. Cultures from the heart gave a pure growth of cocci. Holt27 reports a case from Harris in a child four years of age. The lesion in this instance affected the right side of the heart and was secondary to a cardiac malformation. Another fatal case in a girl fifteen years old is described by Cantley. this case the pilmonary valve was affected. On the other hand, Adams relates a case of recovery as one of only four hitherto reported under the age of fourteen years.§ The greater proportion of cases reported in early life have been over ten years of age. There are 25 or more of these (Holt), and although the right heart is occasionally affected, the disease, according to Lannois and Paris, seems usually to attack the aortic valves. Loeb describes such a case where there were extensive lesions of this valve, and which followed gonorrhœa. The diplococci found had the morphological appearance of gonococci.

<sup>\*</sup> Poynton and Painc. Medical and Surgical Society of London, April 8, 1902.

<sup>†</sup> Year Book, loc. cit. ‡ British Medical Journal, June 13, 1903, p. 1373.

<sup>?</sup> Archives of Pediatrics, December, 1902.

While the authoritative cases of ulcerative endocarditis of rheumatic origin are infrequent, such cases are occasionally described. E. Berie<sup>29</sup> reports two such. The bacillus coli is rarely found and seldom exists as a cause. Still, cases are described both by Henchen

and by Andrews.

The symptoms of malignant endocarditis vary very much in individual cases. Sometimes the signs pointing to endocarditis are very indistinct, or entirely absent. This is true particularly where the cardiac disease complicates another acute infectious and septic disease like pneumonia, empyema, or meningitis. Herzog, O'Donovan, and others report cases which appear to support this position. Not only is the difficulty of recognition very great by reason of the absence of distinctive signs, but also by the variety of clinical symptoms present. The latency of the disease is sometimes such that a diagnosis cannot be made in the beginning.\* Gavala's case is an instance of this sort. In many cases during life there are no cardiac murmurs, and the diagnosis must be based wholly upon the symptoms.† Again, the symptoms may be most misleading and point to a very different disease, as in the two remarkable cases of N. Pitt,30 in which symptoms at first appeared to be those of spinal disease. The complete absence of fever also in a given case is not an absolute reason for calling in question the diagnosis, as witness the fatal one reported by C. O'Donovan, without fever.<sup>31</sup> In very few cases of Glynn's patients were there rigors, and in some pyrexia was absent for days and weeks at a time. It may be remarked that the former part of this experience is certainly almost unique. The difficulties attending the diagnosis are sometimes insuperable, for trustworthy clinical indications may be wanting. (Glynn.)

In other instances where the malignant endocarditis is subacute or chronic, and complicates an endocarditis of rheumatic origin, it may show distinct signs and is quite easily recognized. In the former cases the autopsy alone reveals the nature of the disease.

Occasionally the differential diagnosis between rheumatic and acute infective endocarditis is practically almost impossible. There is a mild form of malignant, non-septic endocarditis which resembles in many particulars the grave form of septic endocarditis. In this form, while the local symptoms are not dissimilar to those of simple endocarditis, the general condition is notably bad. In this form we have hemorrhages of the skin and mucous membranes, and emboli in various organs, and also joint implications. But though the joints are swollen and tender the inflammatory arthritis remains serous; it does not become purulent. In the graver cases of this type the patient will often succumb after a few weeks' illness to an aggravation of the general condition. On the other hand, the milder cases will often recover. The severe malignant form of

<sup>\*</sup> Jackson, loc. cit.

<sup>‡</sup> Strümpell, p. 307.

<sup>†</sup> British Medical Journal, May 19, 1900.

endocarditis is almost invariably of septic origin. It is of distinct etiological origin as compared with the milder form referred to. It is characterized apart from cardiac symptoms by the formation of metastatic abscesses in different organs, with or without the accompaniment of hemorrhages. The malignant endocarditis and the metastatic abscesses are directly referable to micrococci; the parenchymatous swelling and changes of organs are the result of the transport of toxins. The microscopic investigation of the different organs often shows the march of the pathological process and how it originated in small foci where minute vessels are filled with micrococci, which later produce areas of cell necrosis, finally leading to suppuration. Because at times no origin at all is discoverable for this form of disease, it seems very obscure. Again, the disease is occasionally not seen by the physician until its later stages, and hence its diagnosis is rendered even more difficult. Very often a pronounced leukocytosis will help us recognize the disease, but the feature of greatest significance is the finding of micrococci in the blood during life. This has already been accomplished more than once. Further bacteriological investigations in this direction are most desirable. Some of these cases run a very chronic course, and one case is reported by Osler where the disease lasted over a year. The autopsy showed extensive vegetations and ulceration of the mitral valve (p. 704). The fever is not always remittent; it may be high and continuous. The rashes, under certain circumstances, may render the disease liable to be confounded with typhoid fever or cerebrospinal meningitis. The sweating is often most profuse. Jaundice is occasionally present and may render confusion with acute yellow atrophy of the liver possible. Cases, even the most acute, usually last a week or more, and yet the disease has been known to terminate fatally in forty-eight hours.

Ordinarily, malignant endocarditis is an intercurrent or secondary affection of some primary septic process. The symptoms of this primary state should not therefore be confounded with those belonging to one of its localizations. It is, however, frequently most difficult to differentiate them. Many of the febrile attacks, which occur in cases of chronic endocarditis and which are accompanied with grave symptoms, result in ultimate recovery. It is very difficult in these instances to be sure whether these cases belong to the benign or malignant variety of ulcerative endocarditis during the period of the acute attack. The fact of the recovery, of course, argues strongly in favor of the benign form, although the clinical symptoms closely simulate those of the graver diseasc.

As to whether an acute endocarditis will be simple or ulcerative may depend somewhat upon the number or nature of the bacteria transported by the blood. Yet as we find the same bacteria in both forms of disease, this position is not wholly tenable. It seems probable that the particular outcome locally, of the fixation of the

bacteria, will depend more upon their virulence than any other one factor. It is also true that ulcerative endocarditis is liable to attack those persons suffering from exhausting diseases and the different cachexiae. In some cases of ulcerative endocarditis the diagnosis is based mainly on the septic symptoms, and there is little or nothing in the local examination of the heart which will throw light on the case. On the other hand, a suddenly developed cardiac murmur, or a distinct and rapid modification of one already existing and showing previous valvular disease, will have great importance in diagnosis. It is necessary, therefore, in all suspicious cases, to make frequent and careful examinations of the heart, and to note all changes of rhythm which occur. The same is also true of the timbre of the murmur which may change at any time, and from being harsh and loud from the previous lesion may become soft and blowing by reason of the fresh disease which has developed. Combined with the heart symptoms are those of sepsis and embolism. The presence of fever and the numerous petechiæ or hemorrhages are always very significant; these symptoms being rarely combined in ordinary rheumatic endocarditis, sometimes the discovery of some evident cause of the septicæmia will bring light to an otherwise obscure case. Thus a foul vaginal discharge, which may be the result of an abortion in which the neck of the uterus has become

abraded, will in this way prove satisfactory.
While chills, fever, and sweating point to septic fever, they do not fix the diagnosis of ulcerative endocarditis, and this must be done by examination of, and findings in the heart, or else by the changes due to emboli in the organs. Skin, urine, spleen must be frequently examined with this end in view. When other means fail to establish a diagnosis, an examination of the blood should be It is claimed that in most infections there is a decided leukocytosis, but in ulcerative endocarditis this statement is not always correct, according to Neussen, who says there is either an absence or possible decrease of leukocytosis.\* On the other hand, Kelly dwells upon the importance in diagnosis of the presence of a moderate leukocytosis of the polynuclear variety. The latter also insists on the positive result of bacterioscopy of the blood. Likewise he attributes much value to the fact of the great instability of heart action, which may be noted in a very brief period. Some cases of ulcerative endocarditis may be readily mistaken for typhoid fever. In the latter, even though of severe type, hemorrhages in the skin are very rare. Moreover, we have earlier enlargement of the splcen, and pronounced abdominal symptoms, usually like tympanites, diarrhœa, distention, and rose spots. In all doubtful cases we should make the Widal test, and sooner or later we expect to get it in typhoid fever. The presence of this test would also help to

<sup>\*</sup> Babcock. Diseases of the Heart, p. 181.

eliminate acute miliary tuberculosis, with which ulcerative endocarditis might be confounded. Unfortunately, the Widal test is not always absolutely reliable, even when present, to determine the differential diagnosis. One such instance is reported by Mathews and Moir,\* where the Widal test was positive, thus confusing the diagnosis with one of typhoid fever. The autopsy showed that the disease was one of ulcerative endocarditis. Some instances, also, are reported, where the Widal test has proved negative. In other cases there has been a positive Widal reaction, and with different strains from one in twenty to one in two hundred. We thus perceive that this reaction is incapable at times of differentiating between these cases. †33 The serum reaction in the differential diagnosis may be misleading in other instances, notably in septicæmia and acute tuberculosis. (Glynn.) Acute miliary tuberculosis may be differentiated frequently by the presence of tubercle bacilli in the sputum, and also by the preponderance of chest signs over those indicating a heart lesion. I have had one case, unfortunately, of miliary tuberculosis of the lungs under my care, which resulted fatally, in which no tubercle bacilli were ever found, and in which the chest signs were changeable and uncertain for several weeks. In this case there was a soft, blowing murmur at the mitral orifice. There were, however, no hemorrhages of the skin, and no manifest symptoms pointing to emboli in the viscera. At one time there was slight hæmaturia, which made me somewhat suspicious of the renal condition. In a few days this cleared up, and I thought it was explained by renal hyperæmia, due to the febrile nature of the disease. The recurring chilly sensations, profuse sweats, and dyspnæa may occur in both diseases. The loss of flesh and strength may also be marked in both.

The temperature chart is probably more irregular and different in nlcerative endocarditis. Here again I have found it very difficult at times to pronounce in which direction I was carried by its careful consideration. As a rule ulcerative endocarditis may be readily distinguished from malaria by the discovery of the plasmodium in the blood, and also by the greater irregularity of the fever and chills which presents the septic type. In what Osler regards as a very remarkable sub-group of this type, the fever and chills may closely simulate regular attacks of quotidian or tertian ague. In those instances where there has been a previously well-marked malarial infection, the differential diagnosis would become additionally difficult. Again, and despite the affirmation of distinguished observers to the contrary, I have met with undoubted cases of malaria, as I believe, in which no malarial organisms have ever been found, and despite careful and repeated microscopic examinations of the blood by skilled observers.

<sup>\*</sup> British Medical Journal, June 22, 1899.

<sup>†</sup> Thompson. Practical Medicine, second ed., p. 319.

Occasionally chronic endocarditis, accompanied by a fever resembling that of typhoid or remittent fever, may lead to confusion in diagnosis. In these instances, however, embolic phenomena, septic or other, are not found. Moreover, these cases are often prolonged for several months, as in one of Bristow's, cited by Osler. In those cases accompanied with irregular fever, embolic phenomena and physical evidences of recent endocarditis with cardiac distress, and which run an acute course, it is sometimes most difficult to know whether ulcerative endocarditis is present or not. If the case goes rapidly to a fatal termination, as it often does, and we obtain an autopsy, of course the nature of the case can be positively decided. If, on the other hand, the fever, restlessness, cardiac distress, and local signs of heart lesions wholly disappear, and the patient recovers entirely, as in certain recorded instances of gonorrhœal endocarditis (Thayer and Lazear), we may still retain, perhaps, reasonable doubt as to our diagnosis.

The instances which are reported to recover are the less acute forms, and have usually been grafted more than once upon old sclerotic changes of the cardiac valves and orifices. In this category I should be inclined to put some of the gonorrheal cases. These, however, as we know, are diagnosed at times more by cardiac changes than by septic symptoms.\* The mechanical factor in the development of ulcerative endocarditis is not an essential one, inasmuch as the fresh endocarditis does not always arise at the site of the old endocarditis if the latter is present.† The distinction Lenhartz makes between chronic septic endocarditis and malignant rheumatic endocarditis, based on the presence in the former of micro-organisms commonly producing sepsis, is called in question by Litten on the ground of variability of bacteriological conditions, and he states that no distinction can be made on this basis. Stengel finds both classifications unsatisfactory.†

In these instances much importance should be attached to the supposed etiological factor. If it be of the nature of articular rheumatism, chorea, or scarlatina, we would infer that we had to do with an endocarditis of benign type; if, on the other hand, we find in the antecedents some pus infection or focus of suppuration, puerperal processes, bone-disease, etc., we are prone to believe that ulcerative endocarditis has developed. Again, the febrile movement may be wholly absent, or elsc pursue a very mild and regular course. In the latter case it is probably due either to the acute endocarditis of simple type, or to the rheumatic cause. When either

one gradually subsides the fever also disappears.

With the greatest possible care, however, on the part of the attending physician, the diagnosis of ulcerative endocarditis may be mistaken or overlooked, so frequently do the symptoms vary.§

<sup>\*</sup> Allbutt, p. 882.

<sup>‡</sup> Loc. cit.

<sup>†</sup> Lenhartz. Gould's Year Book, 1903, p. 182, § Thompson, p. 319.

Again, as I have pointed out already, there may be a complete absence of recognizable cardiac signs locally. In the acute classes resembling cerebrospinal fever, blood cultures do not help us very much to make an accurate differential diagnosis. If the spinal disease be of tuberculous nature, puncture of the spinal membranes and withdrawal of fluid may be of very great value in revealing the presence of tubercle bacilli. In the non-tuberculous variety, whether it has become suppurative or not, we may find the same organism that is discovered in ulcerative endocarditis, and of course our doubts are in that case not solved by this method of exploration.

The course of ulcerative endocarditis may be very brief. Indeed, it may be a very acute disease, last only a few days, and then terminate fatally. Such are the extreme and relatively rare instances. The more frequent ones are those where the disease has lasted several weeks. Its progress onward and downward may be continuous. On the other hand there may be periods of relative improvement followed by renewed exacerbations. The patients seem to improve for a time and subsequently relapse and return to the hospital in a worse condition. (Glynn.) When death actually occurs it is occasioned by the progress of the heart disease, which finally causes pronounced asthenia. Or again it is the prolonged general sepsis which apparently occasions the fatal outcome. There may be complicating pulmonary cedema or pneumonia, and in this way death occurs more rapidly. Sometimes it would appear that the term of life is closed essentially by reason of emboli in different organs-kidney, spleen, or brain.

An interesting case is reported by Babcock (p. 173 ct seq.) following an attack of tonsillitis which after five months' duration terminated fatally. In this case, although clearly a septic one from the beginning, the pulse persisted at about the same rate (105), and there was a fairly continuous temperature with slight changes. There was present marked bulbous enlargement of the terminal phalanges of the fingers due to capillary dilatation. Unfortunately in Babcock's case there was no autopsy. Credé's ointment and antistreptococcic serum were employed, with the results perhaps of increasing strength for a while, and occasioning a slight reduction of temperature. The occurrence of emboli always renders the prognosis more serious. In addition to the mere mechanical results of these emboli in the different viscera we observe their septic consequences, which contribute to the speedy, fatal termination. Thus we find single or multiple septic abscesses in the spleen, liver, kidneys, and, indeed, throughout the body, and these are the evidences of general infection of the economy. Of course, death is the inevitable result, almost, of such a condition.

In general the treatment of ulcerative endocarditis is that of acute benign endocarditis with even greater precautions exercised about preserving the strength of the heart, noting that independently of the specially destructive tendencies of the disease to the cardiac valves and walls and the formation of abscesses locally in its structure the heart muscle is more likely to suffer from the effects of the toxemia itself than in the relatively benign form of disease. The treatment may be regarded therefore as essentially symptomatic.

To combat general sepsis we should rely upon large and repeated doses of alcohol in the most palatable and useful form—i.e., the best old brandy—alternating it with best champagne now and then for a day or two. The employment of alcohol in septic disease and in sufficient quantity is still heartily endorsed by many eminent clinicians and despite many and strong arguments made use of by its adversaries. Carbonate of ammonia is also possibly a useful adjunct to alcohol for a little while, in view of the thrombotic findings upon the cardiac valves which some autopsies reveal and by reason of the proofs we seem to have, clinically, of its action in lessening somewhat the tendency to such deposits or formations. The late Dr. Benjamin Ward Richardson insists forcibly upon this view as regards certain infectious diseases, notably diphtheria, and I have always believed with much reason. I am satisfied, however, that carbonate of ammonia is far more depressing even than alcohol if too long continued, and particularly in large, frequently repeated doses such as are so often insisted upon in clinical text-books of practice of medicine.

To abate or lessen the chills and the fever quinine is used by some with the idea that it will do so if given in doses of 5 to 10 grains three or more times daily. With our improved knowledge of the etiology and pathology of the disease such a view seems scarcely warranted. And when we think of the cardiac depression which may follow such doses, demonstrated many years ago by Binz, I find no adequate reasons for the use of the drug after this manner. The treatment of disease then, according to many, is practically that of septicæmia (Osler), and except the measures which we should rationally employ in all forms of endocarditis even the mildest.

Are there therefore no known measures which have any curative influence upon the march and termination of the disease itself? Dreschfeld speaks of having been useful by means of a combination of quinine and arsenic in 3 cases, 2 of which he reports.<sup>34</sup> In neither case, however, did recovery take place. Perhaps the prognosis of ulcerative endocarditis may become more hopeful with our improved forms of treatment; more so even than that of the cases of endocarditis which are regarded as relatively and less immediately dangerous.

With the progress of serotherapy and of intravenous medication this statement has become especially true during the past year. This progress is due to researches of pathologists who, like Poynton and Paine, have pointed out the parasitic nature of the disease.

Besides, several histories have been reported pointing to the favorable outcome of the disease through medication. Occasionally recovery may be expected. Clinical reports bear evidence of this, and besides it is more than justified by the results from autopsies.

The treatment of the disease has now definitely in view the killing of the germs. Two methods of medication have been tried—i. e., the sera and the mineral germicides. They may be administered either internally by mouth or rectum, subcutaneously or intravenously. Later all three methods may be combined at the same time to hasten the cure.

As to the relative value of these remedies it is impossible to state at present. But each day seems to show how important has become the interactions between living and inorganic matter. In this line notably are the effects of radium on the tissues. The promulgation of the catalytic action of sera and albuminized metals is also related to our ignorance, but presuming this theory to be correct it would prove how useful the direct application of remedies may be to the cure of disease. An effort has been made to introduce antiseptic remedies in sufficient quantity into the system to exert at least a modifying influence upon the sepsis. (Babcock.) Among these the sulphocarbolate of soda in one-half drachm doses has been used by Sansom, and with such good effect that one patient was enabled to leave the hospital and remain away ten months before a fresh attack occurred. To the latter, however, she succumbed, and the autopsy justified the accuracy of the diagnosis by revealing cardiac valves permeated with micrococci.

Of course if antiseptic medication is to be of real service it must be employed in sufficient amount to affect the system thoroughly, and be continued for a considerable period. And here resides the danger with which we are all familiar, to-day more than ever, that in our efforts to destroy or neutralize micro-organisms and their toxins so pernicious to the economy, we may occasion great harm to the composition of the blood which would more than counterbalance any beneficial results from the use of antiseptic medication. This is especially true if we employ the hypodermic method. In illustration I would refer to the brilliant work of Barrows in the treatment of puerperal septicæmia, who at first seemed to have achieved a very remarkable triumph.

According to the latest laboratory experiments of J. M. Fortescue Brickdale, <sup>35</sup> injection of antiseptics produce no favorable results. This experience is corroborated by W. H. Park and W. A. Payne, <sup>36</sup> who state that in their judgment the use of plain salt and water intravenously will be found equally useful and less dangerons than diluted formalin injections.

On the other hand the use, clinically, of intravenous injections of antiseptics by Netter,<sup>37</sup> Maguire, Landerer, and Ewart, has been at times distinctly favorable. Further, Klotz narrates a case

resulting successfully, in which colloidal silver was used hypodermically. After two injections there were rigors and no improvement; but after the third there was rapid decrease of fever and ultimate recovery.<sup>38</sup>

As Ewart remarks, forcibly, too rigid adherence should not be directed toward mere "germicidal potency" as a test for practical utility. It may be that intravascular antisepsis will prove delusory, but over and beyond is the great subject of intravenous medication which must remain as a very valuable aid to our methods of treatment. Inasmuch as the action of the antiseptic injections is not bactericidal, some other explanation must be given of their power for good. According to Netter this resides in a catalytic action much resembling the action of ferments, and depends upon a mysterious power of matter. In the discussion of Dr. Barrows' paper the majority seem to preserve an open mind as to the desirability of the treatment in any extensive way.<sup>39</sup>

O'Brien<sup>40</sup> has pointed out some of the dangers resulting from intravenous injections—i. c., rigors, collapse, and respiratory embarrassment. In one case sudden death followed. As there was no autopsy a definite explanation could not be given. It is important to note that those who make use of these injections should be pre-

pared to deal with sudden emergencies which may arise.

No doubt there is some comfort to be taken, as Babcock would have us believe, apparently, from the neutralization of the toxins found in the intestinal tract during the course of ulcerative endocarditis, and which doubtless, unless properly neutralized, tend to aggravate the original disease and prevent recovery. Among these so-called antiseptics used to modify favorably autointoxications from the intestinal tract, there are only a few in which I have at present even limited confidence. The best and least harmful which I have tried are small, repeated doses of beechwood ercosote, the salts of bismuth, and wood chareoal. In a paper read before the New York Clinical Society about two years ago I directed attention in this connection to these drugs, and spoke favorably of their use as compared to others I had tried.

Up to the time of writing a certain number of cases have been treated by the antistreptococcic scrum, and with more or less success. There is a certain degree of reason in the use of this scrum, because it appears to be useful in other septic cases—notably puerperal septicemia. It is also reasonable to employ it because streptococci are undoubtedly among the organisms which appear frequently infiltrated, as it were, in the cardiac valves at the autopsy of these cases. The scrum itself, properly employed, does not cause injury to the patient, and again we find in the antitoxin treatment of diphtheria an analogy which makes us somewhat hopeful of this other new treatment. The outlook seems to be, therefore, that pathological scra will probably be more and more

ROBINSON: ULCERATIVE ENDOCARDITIS. used. Antitoxins and immunizing sera have, indeed, more than one action, and, it has been demonstrated, may be useful in distinct diseases. The explanation of their effects may reside in a catalytic action not dissimilar to that of the albuminates of the metals.

action not dissimilar to that of the albuminates of the intravenous route is the one now Preferable for serotherapy.

The intravenous route is the one now Preferable for serotherapy.

To the former intentions describe discontinuous injections have proved ineffective. To the former injections, despite disadvantages and dangers, we should recur hopefully. dvantages and dangers, we should recur nopelluly.

Sir Donglas Powell reports three successful cases from the use of antistreptococcic serum, and emphasizes the fact that if it were of antistreptococcic serum, and emphasizes the fact that it is were employed earlier in the disease, and before a general dissemination of it in different organs had taken place, our results would be better. He also considers that in its use we must not expect benefit where He also considers that in its use we must not expect benefit where present, but be hopeful and limit its use to those cases in which there has be a superfixed by the superfix streptococci or staphylococci have been causative. streptococci or staphytococci nave been causauve. It there be anywhere a purulent focus which surgery can reach it must be anywhere anywhen and entriproceed; if poccilla Othornica wa chould. promptly dealt with and suppressed if possible. Otherwise we should. expect continual accessions from this source of the toxic organisms whose influence we wish to combat. Hence, the employment of Whose influence we wish to compat. Hence, the antistreptococcic serim must remain useless. On the other the annstreptococcic serum must remain usetess. On the other those already in the blood may be other than

though many of those already in the blood may be other than though many of those already in the blood may be other than To obtain our best, most hopeful results treatment should be a compared to diagnosic approaches a begun at an early date, or so soon as the diagnosis approaches a ligh degree of probability. There are, moreover, evident grades in the malignancy of different cases of ulcerative endocarditis, and it is impossible at first to pronounce as to the precise future course of impossible at first to pronounce as to the precise future course of a given case of the disease. The reported cases of improvement of a given case of the disease. The reported cases of improvement foot vormalian we chould be another and from this etand. and recovery under more man one son or treatment makes this stand-Point to begin early treatment with the serum. It is always judicious Point to begut early treatment with the serum. It is always Judicious and advisable also, to take blood in a doubtful case for the purpose and aavisable also, to take blood in a doubling case for the purpose of culture inoculation and other experiment, even though no profitof culture inoculation and other experiment, even though no pronteques of the disease. (Gibson, quoted by Babcock.) Great care hat the hlood obtained for hacteriological examimust be taken that the blood obtained for bacteriological examimust be taken that the blood obtained for discretionogical examination should not be contaminated. The staphylococcus albus, if nation should not be contaminated. The staphylococcus alous, if die to contamination, and is not the specific cause of the most framiently found by disease. The micro-organism which is most frequently found by cultivating the blood is the micrococcus pyogenes. It has been of mornaling and on which and on which it has been to be a control of the micrococcus pyogenes. obtained in many cases of ulcerative endocarditis. If a patient With some valvular disease has irregular temperature, is a name of the blood a with some varyular disease has irregular temperature, is antenue, diagnosis of illogrative and condition cultivation of the blood, a and the indiand sureprococci are obtained from cumivation of the blood, a strong ic to inicat antictrantococia comm. Rload evamination cation is to inject antistreptococcic serum. Blood examination

should not be considered infallible as an aid to diagnosis and prognosis. As Bryant<sup>41</sup> writes in corroboration of Ewing's statement: "The examination having been performed, its results are to be interpreted only in the light of the fullest possible clinical information."

It would appear that ulcerative endocarditis of pneumococcic origin offers little hope for any beneficial result from this treatment. Let us hope that the day is not far distant when a suitable serum will be available for every kind of septic poisoning, no matter what the precise efficient bacterial cause may be. The modern researches of the Klemperer brothers and others give us renewed trust that our wishes may soon be realized. (Babcock.) From 3 cases reported by Babcock he is evidently disposed to make use of the antistreptococcic serum in any future cases he may see, even though the diagnosis may be somewhat doubtful, and provided other treatment has been used in vain. He remarks with justifiable emphasis: "Such cases are so desperate and the prospect of recovery so slight that I believe one is justified in resorting to whatever affords even a chance of benefit; and if an old preparation is employed there is not much danger of producing erythema or articular inflammation, and the remedy cannot prove more harmful than the disease itself, unchecked."\* Successful results in the use of antistreptococcic serum in the treatment of ulcerative endocarditis have been reported by Sainsbury and by Pearce, <sup>42</sup> another also by Clarke. <sup>43</sup> The following case reported by Bryant<sup>44</sup> appears to me very convincing: "A boy, aged fifteen years, was admitted to the hospital suffering from mitral disease. He had had several attacks of rheumatism. His temperature was varied and running an irregular course, ranging between 98° and 101.5° F. When he first came under my care he had been in the hospital for nearly two months, and during the whole of the time his temperature had been raised and he had not had any manifestations of rheumatism or of tonsillitis. A bacteriological examination of the blood showed the presence of streptococci in pure culture. A few days afterward the temperature dropped to normal and remained normal. A subsequent bacteriological examination of the blood was negative. I considered this boy was suffering from infective endocarditis, that the acute process had subsided, and the streptococci died out."

In some cases of ulcerative endocarditis treated with antistreptococcic serum, while temporary benefit may result from its use, the result ultimately has been fatal. An instance of this kind is described by H. M. Cooper.† In this, as in other cases, it was thought if the serum treatment had been instituted earlier a succesful result might have been obtained. Per contra, as regards the matter of the innocuousness of these injections, the following cases are interesting and important. B. M. H. Rogers<sup>45</sup> used five injec-

<sup>\*</sup> Loc. cit., p. 797.

tions of 10 c.c. each of antistreptococcic serum in a case of ulcerative endocarditis, in which pure cultures of streptococcus had been obtained from the blood. The injections caused violent pain, were without effect, and death occurred. Post-mortem cultures yielded streptococci. J. H. Abram<sup>46</sup> reports another case treated in a similar manner after streptococci had also been found in the blood. The case was fatal; but it was found after death that the streptococci had disappeared. The serum is believed to have caused this disappearance.

Cyril Ogle<sup>47</sup> indicates the value of antistreptococcic serum in cases in which the symptoms during life, or the post-mortem findings, showed ulcerative endocarditis. Of course, the cases are not favorable ones in view of the constant passage of the blood current over the surface of the affected organ-i. c., the heart. Still, recovery is not incompatible with this grave infection when thus treated. In Dr. Ogle's table the successes amount to 31.5 per cent.; in Sir Douglas Powell's tables, to 25 per cent.48 On the other hand, Nathan Raw used antistreptococcic serum in 5 cases without any beneficial results. And Glynn reports no information of an encouraging nature from Liverpool hospitals, and without success in 3 of his own cases. I find 1 successful case reported by Moritz,49 in which antistaphylococcic serum was employed. Six injections of 5 c.c. were sufficient to dissipate the acute symptoms. When they were begun the patient had been ill during two months. weeks of treatment the temperature was normal. Six weeks later a heart murmur was present and the pulse was rapid. Still the man remained in good condition. 50 Other methods of treatment have also been followed by reported cures. One by Coleman which followed vaccination. Another from Hepburn in which the treatment was entirely symptomatic. In one instance the aortic murmur disappeared during convalescence. The treatment was by the Brand method and unguentum Credé.<sup>51</sup> Roussell<sup>52</sup> reports three recoveries. Another recovery of gonorrheal endocarditis is from a paper of

The employment of yeast in the treatment of ulcerative endocarditis is referred to by Sir Douglas Powell, and 1 successful case out of 5 is reported by him. In the other case there was no appreciably good result. In one other instance where nuclein was employed there was a decided lowering of temperature. The remedy was employed subcutaneously. If yeast has any remedial value it is probably due to the nuclein or nucleinic acid it contains, as instanced by Vaughn. The latter may be used by mouth, rectum, or hypodermically, according to the strength and kind of preparation made use of. It would seem as though the curative action of the nuclein was essentially due to its power of increasing polynuclear white cells. These, as we know, are frequently more numerous in ulcerative endocarditis, and the germicidal properties of nuclein are explained by their additionally increased number. Many favorable reports, according to Babcock, have been made about the value of yeast-nuclein in the treatment of divers pus infections. And in view of these statements he was encouraged to give it a trial in a case of acute endocarditis complicating a follicular tonsillitis, possibly of rheumatic origin. During the period the remedy was taken the fever slowly abated. Despite this fact, however, the case terminated fatally. Latterly, Duckworth reports, in the Section of Medicine of the Fourteenth International Medical Congress (Madrid, April 25, 1903), a case of probable ulcerative endocarditis in which a treatment with fresh yeast and antistreptococcic serum hypodermically was employed without appreciable benefit. Subsequently, however, a cure was apparently effected by repeated injections per rectum of a mixed antistreptococcic serum, 10 c.c. being the dose employed.\* "This case may be taken," writes Duckworth, "to illustrate the effects of a specially virulent quality or variety of the specific infecting microbe which commonly induces ordinary rheumatic symptoms, and may add support to the view of Poynton and Paine that infective endocarditis may sometimes be a primary affection due to a virulent form of the peccant matter of rheumatism."

If all endocarditis should be properly regarded as infective, it is indicated to find our remedial agent among the class of anti-septic remedies. The most available and least objectionable is the one to make trial of. Amidst the rapidly increasing number of this class of remedies one will be ultimately found that is decidedly curative in many instances. Of course, in making use of the antiseptic remedy so as to influence the entire mass of blood and prevent the infection from being carried to and localized upon the endocardium, we should avoid strictly employing remedies which threaten the general health. At present, moreover, we make use of such remedies mainly in the treatment of the supposed virulent cases, and usually at a later stage of the disease when the outcome is almost surely fatal. In the far larger class of benign cases of endocarditis, and hence the more important ones, their progress is often not stayed by this or any other careful treatment soon enough. The result is they continue their onward insidious and disastrous march. If these cases were treated in the beginning by judiciously selected antiseptic remedies, it is to be hoped that eventually we should have fewer cases of both sorts, and mainly, I believe with Ewart,53 of the ulcerative forms. Further, we should not be obliged to admit, as it seems to me, with the writer of the latest and most valuable treatise on diseases of the heart, "that the most the physician

<sup>\*</sup> Lancet, May 2, 1903, pp. 1268, 1269; and Boston Medical and Surgical Journal, August 29, 1903, p. 238.

<sup>†</sup> British Medical Journal, May 23, 1903, p. 1195.

can do in the treatment of acute endocarditis is to aid nature by helping to maintain the vital powers that lie in nature's way." Let us remember that recovery in an apparently desperate case is possible, and the future may bring improved methods both of serum and antiseptic treatment.

It may be well to add that the latest experiments upon animals seems to prove that the Aronson antistreptococcic serum is superior to the others, notably those of Marmorek and of Tavel. It is apparent, also, that to obtain the best curative effects the serum should be given intravenously. Also, treatment according to this method should be continued well into the period of convalescence, inasmuch as death occurs sometimes when all danger seems to have

passed.

Finally, I would again insist upon the primary importance in all cases of beginning the use of the serum at an earlier date than hitherto has usually been done. Sometimes, not to say frequently, it has been employed when all curative methods must prove futile, as the economy is unable to respond favorably to that as to all other medication. Moreover, whenever the infection has lasted more than a very brief period much larger doses of serum are rendered necessary to produce similar curative effects. I shall not attempt to explain how the serum acts. Nor, indeed, is it positively known. Certainly it has no appreciable effect upon the growth of cocci in the culture tube, and it appears in final analysis merely, so far as our knowledge now extends, to diminish virulence, "for cocci which have been left for some time under the influence of the serum will no longer bring about hæmolysis."35 The latest paper on the use of "antistreptococcic serum in the treatment of inflammatory rheumatism and other diseases" is to my mind very encouraging. It shows conclusively it is most efficient when given carly in infectious disease; also, that it is useful in diplococcic infection. In Dr. G. H. Sherman's cases "none of the patients developed heart complications, and complete recovery took place in a comparatively short time." This statement contradicts that of Osleri.e., "We know no measures by which in rheumatism the onset of endocarditis can be prevented."\*

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- 6. Progressive Medicine, September 1903, p. 79.
- 7. Practice of Medicine, 6th ed., p. 595.
- S. C. S. Bull. Medical Record, December 20, 1902.
- 9. Johns Hopkins Hospital Bulletin, October, 1902.
- 10. Progressive Medicine; also Deut. med. Woch., May 22 and 29, 1902.

- 11. To show the extreme rarity, even with typhoid fever, I would cite Dr. Osler's medical clinic at the Johns Hopkins Hospital, where there never has been a case (written communication from Dr. W. S. Thayer, December 10, 1903). Very probable cases, in view of the symptoms during life, are occasionally met with. Even in fatal cases with characteristic symptoms, where no autopsy is obtained doubt as to diagnosis may be urged, although in one of Dr. Thayer's cases such doubt would hardly be justified.
  - 12. Wells says this complication is very frequent.
  - 13. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1901, p. 53.
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  - 17. Journal of the American Medical Association, August 19, 1900.
  - 18. Progressive Medicine, September, 1903.
  - 19. Gould. American Year Book of Medicine and Surgery, 1903, p. 752.
  - 20. Progressive Medlcine, September, 1902, p. 128.
  - 21. Allbutt's System of Medicine, vol. vi. p. 876.
  - 22. Practice of Medicine, 4th ed., p. 701.
- 23. The vegetations themselves, although unrecognized during life, may have been present for a long while, as shown by autopsy.
  - 24. Dessy. Boston Medical and Surgical Journal, September 1, 1898.
  - 25. Journal of Experimental Mcdicine, January, 1899.
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  - 27. Diseases of Infancy and Childhood, 2d ed. p. 622.
- 28. The exceptions to this rule would appear to be cases of gonorrheal origin where the right heart is frequently involved (Thayer and Lazear).
  - 29. Semaine méd., January 21, 1900.
  - 30. Practitioner, November, 1898.
  - 31. Medical News, July 23, 1898.
- 32. The duration in the fatal cases is only a few days or weeks, but in those that recover it is usually much more prolonged.
- 33. According to MacFarland there was in 4000 cases only 4 per cent. of error (Babcock, p. 182). If after sixth day of illness test is negative, typhoid fever may be properly excluded (Allbutt, foot-note).
  - 34. Alibutt's System of Medicine, vol. vi. p. 884.
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  - 40. Lancet, October 11, 1902.
  - 41. Ibid., February 7, 1903, p. 364.
  - 42. Ailbutt's System of Medicine. Loc. cit., p. 885.
  - 43. Lancet, July 21, 1900.
  - 44. Ibid., February 7, 1903, p. 364.
  - 45. 1bid., June 10, 1899.
  - 46. Ibid., February 25, 1899.
  - 47. 1bid., March 14, 1903.
  - 48. Ibid., April 25, 1903, p. 1153.
- 49. Serum therapie bei Endocarditis Maligna, St. Petersburger medicinische Wochenschrift, 1898.
- 50. In Moritz's case the diagnosis of the organism present had not been confirmed previously by a blood examination, although the evidence of implication of the valves seems to have been certain (Lancet, March 14, 1903, p. 723).
  - 51. Philadelphia Medical Journal, January 12, 1901.
  - 52. 1bid., February 23, 1901.
  - 53. Progressive Medlcine, September, 1902, p. 112.
  - 54. Babcock, p. 193.
  - 55. Medical News, September 5, 1903, p. 462.
  - 56. American Medicine, October 17, 1903, p. 633.

Note.—Owing to the length of this paper, I am obliged to omit the histories of my cases.

In Bullctin of the Ayer Clinical Laboratory of the Pennsylvania Hospital, October, 1903, a unique case is reported of ulcerative endocarditis caused by Weichselbaum's meningococcus.

### REMARKS ON GASTROSUCCORRHŒA AND TETANIC ATTACKS OCCURRING WITH CHRONIC ULCER OF THE STOMACH.<sup>1</sup>

By J. KAUFMANN, M.D.,

Ever since analyses of gastric contents have been made in order to study the function of the stomach and its disturbances mistakes have been made chiefly in two directions: certain functional disturbances which are really only symptoms have been stamped as diseases, and in explaining certain conditions too much stress has been laid upon secretory disturbances, the importance of motor disorders being underestimated. This applies also to the picture described as gastrosuccorrhea. Although much has been written about this symptom-complex, there is still a great deal of confusion in regard to its correct interpretation, and it is therefore justifiable to consider once more whether this picture ought to be taken as an independent disease.

Reichmann was the first to apply the name "gastrosuccorrhœa" to a set of symptoms which are chiefly characterized by the presence in the fasting stomach of a fluid possessing all the chemical and physiological properties of gastric juice. The patients, who are generally emaciated, complain of pyrosis, eructation, and vomiting of highly acid matter, and suffer a great deal from gastric pains coming on after meals and during the night. Examinations of the stomach contents after test meals show hyperacidity and impaired digestion of starches. In the urine there is often a diminution, and sometimes even a total absence, of chlorides. In Reichmann's opinion the characteristic feature of this condition is the continual flow of gastric juice, not only after meals and during the process of digestion, but also during the intervals when the stomach of a normal individual should be empty.

Reichmann's publication aroused an extensive and lively discussion of the questions: Is gastrosuccorrhæa, as its name indicates, really a primary secretory disturbance, or is the accumulation of secretion in the fasting stomach the result of a motor insufficiency? Is gastrosuccorrhœa a disease per se, or is it merely a peculiar combination of symptoms which accompany other already well-known pathological conditions? A consensus of opinion on these questions has not as yet been reached.

There are two varieties of gastrosuccorrhoea—the periodic and the chronic. In the *periodic form* we have to deal with attacks of vomiting of gastric juice, coming on spasmodically and lasting from

<sup>1</sup> Read before the German Medical Society of the City of New York, April 8, 1902.

a few hours to several days. The condition has been attributed to a morbid overactivity of the secretory nerves of the stomach, which is regarded as a neurosis by itself, as a symptom accompanying hysteria or neurasthenia, or as a symptom occurring in the form of gastric crises in tabes and other spinal diseases. The remaining symptoms occurring with such attacks, pyrosis, headache, gastric pains, and vomiting, are classed as secondary manifestations. The same attacks have, however, been described by a number of other writers under different titles, the name depending upon the symptom regarded as being the most important. Thus, Leyden refers to them as "periodic vomiting;" Struebing classes them with disorders which he designates as "angioneurotic ædema;" Rossbach, who considers the increased secretion of hydrochloric acid as the chief factor in the condition, calls them "gastroxynsis." They are also found in descriptions of nervous diseases. Möbius, for example, associates them with migraine. I shall not further discuss this group of cases of periodic gastrosuccorrhoea, the pathogenesis of which is still very vague. The secretion of large quantities of gastric juice accumulating in the stomach independently of the ingestion of food may play an important role. However, all that has thus far been taught about the relation of the various symptoms to one another, and especially in regard to the point whether this increased secretion of gastric juice is the primary or only a secondary factor in the attacks, is still altogether hypothetical.

In chronic gastrosuccorrhæa the conditions are entirely different, since it is not of a nervous character, but is dependent upon anatomical changes of the stomach or duodenum. In these cases it can be demonstrated that the presence of fluid in the fasting stomach invariably means a motor disturbance, and that the view that chronic gastrosuccorrhæa is a disease per se is not well supported.

As has already been mentioned, Reichmann's theory was that the characteristic feature of the disease was the presence of gastric juice in the stomach at a time when the organ should be empty. According to his view, this accumulation of gastric juice occurs because the mucosa of the stomach secretes continuously without any apparent irritation, but solely in consequence of the morbid activity

of the secretory nerves of the stomach.

Reichmann, however, did not overlook the fact that the presence of gastric juice in the fasting stomach could not be explained simply as a hypersecretion. In some of the cases described by him as much as a litre of fluid rich in hydrochloric acid could be expressed in the morning. In these cases there was undoubtedly an increased secretion, but this is by no means the rule. In a number of other cases the quantity found was decidedly less. The amount of hydrochloric acid contained in the fluid also varies. In cases where only relatively small quantities are found, or where the amount of hydrochloric acid is low, we cannot very well speak of increased secretion,

especially as we do not know the quantity secreted by the normal stomach during a given time. The essential point, therefore, is not that there is an increased secretion, but is rather in the fact that this secretion is found in the stomach at a time when the organ

ought to be empty.

The opinion was formerly held that the fasting stomach of a healthy individual was entirely empty. This view has since been somewhat modified, Rosin and Schreiber having reported that in systematically examining a large number of healthy individuals they often found gastric juice in the fasting stomach in varying quantities, sometimes reaching 40 c.c. Martius, Hemmeter, and others have confirmed these statements. The gastric secretion in these cases is explained as being the result of the stimulation caused by swallowed saliva and pharyngeal mucus.

However that may be, quantities of 50 c.cm. and over are surely pathological. Where such quantities are found it is possible that gastric secretion has been increased and kept up beyond the time required for digestion. But the fact that it is found in the fasting stomach can only be explained by the existence of some hindrance to its passage into the intestine. For, if motor function of the organ is normal, there is no reason why such increased sccretion should not pass into the intestine just as well as other stomach contents.

The misinterpretation of these conditions was partly due to the singular confusion which followed the discussion of the meaning of gastric dilatation. I shall not enter into the discussion of this subject further than is necessary for understanding its relation to gastrosuccorrhea. There is no reason for discarding the old, well-defined clinical picture of gastric dilatation. Its characteristic feature is that it is a combination of two conditions which must be distinguished: the enlargement of the organ and the stagnation of stomach contents. Enlargement of the stomach is an anatomical condition. Stagnation of stomach contents represents a functional disturbance—a motor insufficiency. A stomach with normal motor activity, no matter what its size, empties its contents during the night. Where this is not accomplished motor insufficiency is present.

The stagnating material may consist principally of solid food remains mixed with a larger or smaller quantity of fluid, or it may be chiefly fluid containing few or no solid particles. When solid particles are found, all authorities agree on the presence of stagnation. But when only fluid can be expressed from the fasting stomach, as is often the case in gastrosuccorrhea, some authors maintain that the condition cannot be considered a stagnation, because no solid particles are contained in the fluid. To support this view, it was argued that in some of these cases certain symptoms generally associated with gastric dilatation were absent. It was claimed, for instance, that in cases where no lowering of the greater

curvature could be demonstrated there could be no dilatation of the organ, and therefore no motor insufficiency.

In diagnosing dilatation of the stomach we must separately consider three things: (1) the size of the stomach; (2) its position, and

(3) its mechanical ability.

Size and position of the stomach do not necessarily indicate its mechanical ability. A stomach may be very large and its greater curvature may be low, yet it may be motorily sufficient. In such a case we cannot speak of dilatation, but simply of a deeply situated, enlarged stomach-megalogastria. On the other hand, a stomach may be high and its motility be insufficient. This very condition is not infrequently found with gastrosuccorrhea. We shall see later on that in these cases we have to deal with gastric ulcer. When the ulcer is situated at the lesser curvature and there are adhesions to the surrounding tissues, the stomach remains high, and in case of dilatation extends upward. In these cases I have frequently seen the fundus of a stomach almost reach the axilla in the dorsal position. When the lesser curvature is thus fixed the greater curvature may remain above the umbilical line, even in cases of pronounced dilatation with decided stagnation of the stomach contents. Hence, a high position of the greater curvature cannot be regarded as proving that in a given case no gastric dilatation is present, and, therefore, no motor disturbance.

Just as invalid is the argument that in certain cases of gastrosuccorrhea no motor insufficiency was present because certain forms of fermentation were absent, particularly the gas fermentation. It is true that whenever there is stagnation in the stomach fermentation sets in. There are, however, various fermentations in the stomach, brought about by different organisms and leading to different fermentation products. The absence of any one form does not indicate that all fermentation is absent. By careful analysis some form of fermentation can always be demonstrated.

As for the statement that a motor insufficiency cannot be present when the stomach contents expressed in the morning do not contain food particles, it must be said that actual findings do not justify this conclusion. Reports of autopsies in such cases, where only fluid could be obtained without food particles, showed pyloric obstruction with ulceration. Also, it must be remembered how difficult it is to empty the stomach entirely when dilatation is present.

We may add that in the majority of cases this fluid actually contains food particles. If we examine the histories of typical cases, as reported by Reichmann and others, we find it especially stated that the fluid expressed from the fasting stomach contained varying amounts of food particles, principally starches, and also sarcine, which, beyond doubt, indicate motor insufficiency.

From the foregoing statements, therefore, we see that all argu-

ments brought forward to explain the presence of larger quantities of gastric juice in the fasting stomach merely as a result of secretory disturbance without motor insufficiency are invalid. We must insist that the accumulation of acid fluid in the fasting stomach is always the result of motor insufficiency. This motor insufficiency may be due to atony of the stomach or to organic or spastic stenosis at its outlet.

Let us now consider the question: Is chronic gastrosuccorrhœa a disease per se? The fact that the presence of gastric juice in the fasting stomach always means a retention of secretion due to motor insufficiency does away with one argument often put forth in support of the theory that gastrosuccorrhoea is a primary and independent secretory disorder—the argument that the secretion of gastric juice takes place without the influence of direct irritation (stimulation by food), but purely as the result of the pathologically increased activity of the secretory nerves. For even small quantities of food particles are sufficient stimuli for the secretion of gastric juice, particularly when they lie directly on an ulcer, and when nothing but fluid is retained this stagnating fluid acts as an irritant. more sensitive the mucous membrane the greater the quantity which it will secrete. The constant irritation of this stagnating fermenting fluid must in time increase the irritability of the mucous membrane and lead to anatomical changes.

Examinations of the mucous membranes in these cases, made at first by Korzynski and Jaworski, and later by Hayem, Hemmeter, Strauss and others, show a definite form of gastritis characterized by a destruction of the chief cells, the parietal cells remaining intact. There was often found a proliferation even up to the formation

of polypi.

In opposition to the view which considers the gastritis a result of the permanent irritation by the stagnating masses, due to the motor insufficiency, some authors claim that the gastritis is the primary element of the whole process, and assert that the inflammation of the mucosa alone suffices to cause an abnormal irritability and an increased and continuous secretion of gastric juice. Even the development of gastric ulcer is attributed to this gastritis.

Granting that the gastritis plays an important part here, it seems to me that there is no reason for dwelling on the question whether the motor insufficiency or the inflammation of the mucous membrane is the primary disturbance. Both are factors in producing gastrosuccorrhœa; in some of the cases the motor insufficiency being the primary trouble, in others the gastritis.

However gastrosuccorrhoea is brought on, since we have seen that gastric juice in the fasting stomach always means a motor insufficiency, there can be no doubt that the stagnating secretion keeps up and increases the inflammation of the mucous membrane.

It is clear from the above explanation that where motor insuffi-

ciency and increased secretion go together a retention of gastric juice can take place. Such simultaneous occurrence of motor and secretory disturbance is often found during the course of various diseases of the stomach. Thus the presence of the gastric juice in the fasting stomach is a condition frequently observed in gastritis acida with atony, atony with secondary gastritis and hypersecretion, pyloric and duodenal stenosis resulting from adhesions or compressions, etc. It is obvious that in all these diseases gastrosuccorrhea can only be considered as a symptom.

Some authors apply the term gastrosuccorrhoea to all cases where gastric juice is found in the fasting stomach. Others maintain that we ought to distinguish between the cases where the presence of gastric juice in the fasting stomach is only a symptom, and another well-defined group of cases for which they would reserve the term gastrosuccorrhoea. They claim that the presence of gastric juice in the fasting stomach does not justify a diagnosis of gastrosuccorrhoea unless the completely developed symptom-complex of Reichmann is also present. They regard this symptom-complex (Reichmann's disease) as a sharply defined, typical picture, showing, besides the characteristic presence of hydrochloric acid in the residual fluid, a number of other symptoms—pyrosis, vomiting, loss of flesh, and, most important of all, of severe pains occurring after meals and during the night.

If we now scrutinize this limited group of cases, in which the symptom-complex of Reichmann is fully developed, it must be said that even for this group no proof has yet been given that gastrosuccorrhea occurs as a disease per se. In fact, whenever an operation or an autopsy has afforded an opportunity to gain an anatomical basis it has revealed ulcer or its sequelæ. Thus we see that even in these cases, which apparently are so well defined, gastrosuccorrhea is only an accompanying symptom of a well-known disease—

i. e., gastric ulcer.

As long as we have no proof that gastrosuccorrhoa may occur as an independent disease we shall do well to regard it merely as a symptom. In this smaller group of cases in which the combination of symptoms given by Reichmann is completely developed and where severe gastric pain plays an important role, we shall not err if we regard it in every case as a symptom of gastric ulcer. If we look upon gastrosuccorrhoa in this light as a symptom, it becomes a valuable aid in diagnosing certain cases of gastric ulcer. Whenever we find a patient suffering from gastric pains coming on regularly after meals and especially at night, with or without vomiting, the presence of acid fluid even in small quantities in the fasting stomach indicates ulcer of the stomach. Hemorrhage and perforation, the most characteristic symptoms of ulcer, are observed only in a certain percentage of the cases. In the remaining cases gastric ulcer may present many different clinical forms, among which

Reichmann's symptom-complex stands out as a very characteristic

and typical picture.

As a rule, in cases which develop gastrosuccorrhœa the ulcer is situated near the pylorus and causes a mechanical obstruction, generally by spasm of the pylorus. This spasm, which brings on severe pain, usually occurs after the greater part of the stomach contents have passed into the intestines. That frequent spasms do really occur here is proved by the finding of a strongly hypertrophic pyloric ring.

In the treatment of gastrosuccorrhoea it is of great practical importance to have clearly in mind the fact that the motor disturbance plays a more important role than the secretory, and, further, that the well-developed symptom-complex of Reichmann is not a disease per se, but a symptom of gastric ulcer. We accordingly treat the condition by freeing the stomach from its stagnating contents, also using methods usually resorted to in gastric ulcer. Cures by such treatment have often been reported, and my own experience is corroborative.

In cases which do not yield to methodical internal treatment for ulcer one should not hesitate to do away by operative interference with the hindrance at the pylorus, which is really the principal cause for the whole trouble. We are more apt to come to this decision when we are certain that we have to deal with ulcer and pyloric obstruction than when we regard gastrosuccorrhea as a disease per se, caused simply by an increased irritation of the mucous membrane. In the literature there are descriptions and post-mortem reports of fatal cases of gastrosuccorrhœa which give one the impression that had the cases been diagnosed as ulcer with pyloric stenosis, and promptly operated upon, the patient could have been saved. In all the cases with Reichmann's symptom-complex which have come under my own observation and which were operated upon, the diagnosis of ulcer was confirmed.

I wish to describe one case in detail because it presents another interesting condition with which gastrosuccorrhea stands in intimate

relation, namely, tetanic attacks.

In May, 1898, the patient, aged forty-four years, stated that for the past two years he had suffered with heartburn and gastric pain of a dull and at times even intense character, occurring several hours after eating, but particularly at night. In the morning, before eating, he was troubled with a gnawing sensation in the stomach and gaseous distention; no vomiting; bowels regular. The trouble had been regarded as nervous dyspepsia and treated as such.

The patient was tall, thin, had a long thorax with healthy thoracic viscera, a flat abdomen and normal outlines for liver and stomach, the pyloric end being painful to pressure. Urine now and later throughout the whole course of the disease free from albumin and sugar and contained a moderate amount of indican.

Examination after test meal (tea and toast) showed moderate hyperacidity with impaired amylolysis. Alkalies and a suitable diet relieved the subjective symptoms for a few months, during which time patient gained six pounds. In the fall the symptoms returned with increased intensity, particularly the pains during the night.

Stomach analysis of November 19th showed strong hyperacidity. As ulcer had been suspected from the beginning, a treatment for ulcer was suggested, but again refused, as formerly. The patient did not place himself under treatment until the end of January, 1899, when the pain became so intense that it robbed him of sleep.

The first lavage (February 16th) showed a black fluid without food particles in the fasting stomach, so that there could be no more doubt as to the presence of an ulcer. From then on rest in bed. For four days nourishment exclusively by rectum—then in the morning Carlsbader Mühlbrunnen and, besides the enemata, milk

per os, at first in small quantities, gradually increasing.

Since three weeks of this treatment gave but little relief from pain, and alkalies, bismuth, belladonna, codeine only relieved the patient temporarily, lavage was taken up and after the washing bismuth was introduced. The fasting stomach nearly always contained from 50 cm. to 100 cm., and occasionally more, of a strongly acid fluid, mostly stained with blood and often mixed with some remnants of food of the previous days.

The bismuth treatment alleviated the pain but little. Irrigations with silver nitrate (1:1000), which were begun two weeks later, also produced little effect. Changes in the milk diet (cooking with fine flour, peptonizing, sour milk) and a trial of thick gruels and soups gave no better results. On the contrary, during the second half of March the pain increased in intensity and duration. Since the rigidly applied internal treatment failed absolutely, operation was advised on March 24th, but had to be postponed several days for ulterior reasons.

During this time there was a decided change for the worse. Until then the quantity of fluid found in the fasting stomach had been relatively small, even when larger quantities had been ingested. During the middle of March, with the increase of pain, the amount of stagnating fluid became greater. From the 24th to the 29th signs of complete pyloric obstruction set in, with almost continual excruciating pains. Although smaller quantities of food were taken the amount drawn from the stomach increased; rapid diminution of urinary secretion, which so far had been plentiful; skin dry; emaciation more marked. Now, for the first time, a hard, painful resistance could be felt in the pyloric region.

March 25th. But little nourishment was taken; during the night, after most violent pains, for the first time there was vomiting of

blood-stained fluid. In spite of the large quantity of the vonitus, and although nothing had been taken afterward, 750 cm. of fluid were withdrawn from the stomach in the morning of March 26th. During this day the patient took only 180 c.c. each of milk and Vichy. Yet in the evening, when the continual severe pain made it necessary to again introduce the stomach-tube, as much as 1100 c.c. of blood-stained fluid was obtained—that is, three times the quantity taken during the whole day. Upon standing a thin, reddishfilm formed on the surface of this fluid, the remainder consisting of clear, light green liquid, with a very high percentage of hydrochloric acid.

During this last introduction of the stomach-tube violent vomiting set in, and with it appeared tonic spasms of arms and legs, both being stiffly extended, the fingers in obstetrician's position. The spasm lasted several minutes. Feeling of numbness in the extremi-

ties. Trousseau's phenomenon negative.

27th. A total of 600 c.c. of milk was ingested. In the evening a litre of sanguineous fluid of intensely acid reaction was removed. During the withdrawal of this fluid through the tube (this time without vomiting) both upper extremities became tonically extended, the fingers of the left hand were extended, those of the right in the position of a penman. The spasm relaxed slowly several minutes after the washing was finished. Lower extremities not affected this time. Trousseau's phenomenon negative.

28th. Condition improved. Pain diminished. Larger quantities of milk taken, and it passed into the intestine. Urinary secretion

again reached 1000 c.c.

29th. Patient was taken to Dr. Lange's clinic. Lavage of the stomach at 11 A.M. One hour later sudden violent pain in the gastric region and symptoms of collapse. Pulse small; face pale; syncope; abdomen drawn in; liver dulness normal. All the abdominal muscles rigid as boards, several fibres standing out as sharp ridges above the level of the skin. Less pronounced cramps in the muscles of the trunk and extremities. The extremely painful tetanic contraction of all the abdominal muscles remained unchanged for hours, despite the injection of morphine and a mild anæsthesia from ether and chloroform.

Four hours after the perforation laparotomy was performed. The anterior wall of the stomach showed a flat, almost circular swelling, about 5 cm. in diameter, its firm edges extending downward to the greater curvature, and its right limit being still several centimetres removed from the pylorus. The serous covering of the swelling lay free in the peritoneal cavity, only its median edge being adherent to the omentum. Exactly in the centre of the swelling was a sharpedged opening of the size of a pin-head; there was some turbid fluid in the neighborhood of the perforation.

A segment as broad as a hand was resected, which included the

antrum pylori and the pylorus; suture of the stomach end; duodenal end joined to the posterior wall of the stomach by a Murphy button. The resected piece, cut open along the lesser curvature, showed on its inner surface an ulcer as large as a fifty-cent piece, with an uneven terraced surface, a very thin floor, and firm, undermined, wavy edges. Cut surface through this edge showed firm, white lines. Microscopically, adenocarcinoma. The pylorus thickened but patent. Microscopic examination of the pylorus showed greatly hypertrophied muscles, but no signs of carcinoma.

The healing of the wound progressed smoothly. Nourishment at first per rectum. Upon giving food by mouth recurrence of pyrosis and pain in the stomach; perhaps this can be partly accounted for by the retention of the Murphy button. These complaints, which were somewhat relieved by alkalies and washing of the stomach, manifested themselves after each meal, no matter what kind of food had been taken; and they continued to disturb the patient in the most annoying manner during the following months almost up to

the time of his death.

An examination after test breakfast on May 25th again revealed considerably increased gastric secretion. Repeated examinations made after this date showed the continuance of hyperacidity for a remarkably long period, in spite of the development of metastatic tumors.

During the first few months following the operation the patient recuperated and gained in weight. In September the pyrosis and pain became worse again; all attempts to influence the secretion medicinally by means of alkalies, bismuth, atropine, etc., were fruitless.

At the end of September signs of decided stagnation set in, with intense pain and vomiting, so that stomach washings were again resorted to and continued until death, on November 19th, at first once a day, then with increasing stenosis, both in the morning and at night. Upon resuming the lavage the tendency to tetanic spasms recurred, and they were more or less pronounced until within a few weeks before death. They generally manifested themselves in extension of the fingers and hands, more rarely of the arms and legs, and lasted at times only half a minute, but occasionally several minutes.

As early as the end of May—two months after the operation—a distinct resistance could be felt at the umbilicus, and four weeks later hard masses were palpable in the abdomen to the right of and below the scar. They grew to be larger than a fist, pushing the abdominal wall forward. On September 23d, when these tumors had already gained very considerable size, the stomach contents still showed a very high percentage of hydrochloric acid. From the middle of October, however, the quantity of this acid decreased rapidly, and lactic acid appeared. From the end of October the large, fermenting residual masses smelt foul, almost fecal.

EPITOME. We have to deal here with a case of gastric ulcer which became carcinomatous in a comparatively short time. To be sure, the duration of the ulcer cannot be accurately determined. The symptoms of which the patient complained for several years had been regarded by competent physicians as manifestations of nervous dyspepsia. Cases of gastric ulcer which are diagnosed as nervous dyspepsia are by no means rare, and here we have another instance of it. But here, as in many other cases, it was the persistency of the pain that aroused the suspicion of the ulcer, which suspicion proved perfectly justifiable when lavage of the stomach showed sanguineous contents. Yet this ulcer had certainly existed some time before this proof was obtained, and had already involved the deeper layers of the stomach, for the operation, performed only six weeks later, showed an ulcer involving the whole thickness of the gastric wall, with firm, undermined edges, which had already undergone carcinomatous degeneration.

On looking back over the history of the case, therefore, we will not err if we presume that all the symptoms which the patient showed during the last three years of his life, including those taken for nervous dyspepsia, were caused by this ulcer, since during all that time the pains varied only in intensity, their character remaining

the same throughout.

At the operation we found that the ulcer was situated several centimetres from the pylorus; the pylorus itself was patent and free from carcinoma, but showed greatly hypertrophied muscles.

This hypertrophy can be explained as a result of the frequent spasms which evidenced themselves clinically by the severe pains. The spasms occurred particularly during the night. For how long a period they had caused stagnation of the gastric juice, with or without food remains, cannot be determined, since for a long time the patient refused lavage. When we commenced to evacuate the stomach regularly in the morning the patient had already been in bed for weeks, living exclusively on a milk diet. In spite of these favorable circumstances, there were nearly always found in the fasting stomach quantities varying from 50 c.c. to 100 c.c. of very acid fluid, often containing food particles. Later the residual fluid became greater when the increase of pains in duration and intensity indicated longer spasms, and shortly before the perforation took place there set in under almost unceasing pains long-continued spasms, which caused extended periods of pyloric obstruction. was this protracted period of pylorospasm which brought about the retention of the large quantities of excessively secreted gastric juice.

When cases like the one just described are considered without prejudice there can be no doubt that the main cause for the accumulation of such large quantities of gastric juice is given in the spastic stenosis which prevents the passage of the secretion into the bowels.

The more severe and the longer the duration of the spasm the larger the amount of fluid.

Tetanic Attacks. When the spastic stenosis in our case became more pronounced and large quantities of stagnating gastric juice were vomited or removed through the tube, tetanic attacks set in. These recurred in a milder form several months after the operation, when the increasing stenosis at the outlet of the stomach again required lavage. We find the same conditions in nearly all the cases of gastric ulcer with pyloric stenosis in which tetany develops: there is always the evacuation of large quantities of gastric juice, either by vomiting or through the tube. This points to the possibility that the withdrawal of such large quantities of chlorine which are not replaced causes certain changes in the system predisposing to the occurrence of tetanic attacks. We shall discuss this point later on.

In our case, as in many others, it was the lavage which furnished the direct irritation which reflexly brought on the spasm. Remarkable, however, is the severe and long-continued tetanic contraction of the abdominal muscles in connection with the perforation. Contraction of the abdominal muscles is, indeed, a well-known symptom of perforation into the abdominal cavity. In this case, however, where a strong tendency to spasm, perhaps due to the deficiency in chlorine, already existed, the perforation was the exciting cause for an extremely severe tetanic contraction of the entire abdominal wall.

It was Kussmaul who, in his famous article on the treatment of gastric dilatation by means of the stomach-pump, first described the occurrence of muscular spasm with pyloric stenosis. In some of these cases we have to deal with true tetany, which, as is well known, is characterized by increased mechanical and electrical irritability of the nerves and muscles. Other cases only resemble tetany, or else are epileptiform convulsions with loss of consciousness. cases described by Kussmaul were pyloric stenoses, in which the frequent vomiting of large quantities of fluid led to a high degree of emaciation and decrease in the quantity of urine. He attributed the convulsions to the diminution of water in the organism, which was brought about by the vomiting of such large quantities of fluid and which led, as he reasoned, to the drying out of the nerves and muscles. This theory was not considered entirely satisfactory. was claimed that there are other diseases of the gastro-intestinal tract in which an abundance of water is lost without the advent of tetany, and that in cases of tetany the introduction of water into the rectum did not prevent the attacks. Other explanations were, therefore, looked for.

Germain Sée believed that the convulsions were caused reflexly by the irritated nerves of the gastric mucosa. This so-called "reflex theory" explains only how the convulsions are brought on, without mentioning the predisposing element. We must remember, however, that the exciting cause, which may be of various characters, is only a secondary element; in order to bring on a tetanic attack a change in the irritability of the nervous system is required and is

really the underlying cause of the whole trouble.

This predisposing element finds more consideration in a third hypothesis, which, thoroughly in accord with modern teaching, attributes the origin of the attacks to autointoxication. This theory is mainly advanced by French authorities, who assume that decomposition-products are formed in the stagnating stomach contents, which, when absorbed, act deleteriously upon the nervous system, and in this way lead to attacks.

However, in spite of diligent research, no one has yet been able to demonstrate such poisons, and Friedrich Müller, a supporter of the reflex theory, points out very correctly that tetany appears, not in cases where the fermenting stomach contents are finally absorbed, but only in those in which the stagnating masses are removed from the system either by vomiting or layage.

Since the removal of great quantities of fluid from the body is actually the only objective finding which is regularly observed in these cases, it remains, after all, the most important point, and if properly interpreted, gives us a better insight into the origin of tetanic attacks than the purely hypothetical autointoxication theory.

Thus, going back to Kussmaul's first explanation, we must say, as this keen observer rightly maintained, that the great loss of fluid by vomiting or lavage brings about the changes in the system which cause the tetanic attacks. We would add, however, that these discharges deprive the system not only of large quantities of fluid, but also of large amounts of chlorides. For in these cases of gastric dilatation complicated with tetany we often find enormously increased gastric secretion. Since, as we have seen in the beginning, the pyloric stenosis prevents the excessively secreted gastric juice from passing into the intestine, it is removed by vomiting or lavage, and thus great quantities of hydrochloric acid become lost from the system instead of being again resorbed.

Bouveret and Devic claim that gastric tetany is observed exclusively in such cases of pyloric stenosis as are accompanied by excessive hypersecretion. This is not absolutely true. Though the instances are very rare, Fleiner, for example, reports cases in which no increase of gastric secretion was found. We will not investigate now the cause of tetany in these particular cases. Suffice it to say that in gastric tetany, as is the case with other spasms, different factors may contribute to the development of the attacks. In the majority of cases, however, it is a fact that large quantities of chlorine are lost from the body by the removal of the excessively secreted gastric juice. This is proved by the fact that in these cases the secretion of chlorine through the urine steadily diminishes, and

finally ceases altogether.

To be sure, the disappearance of chlorides from the urine here is not an absolute indicator of the quantities really lost from the body. The organism holds on to its chlorine obstinately. When we limit the supply of chlorine by cutting it out of the food the quantity excreted in the urine becomes less, and finally disappears altogether. At the same time the secretion of hydrochloric acid with the gastric juice will stop, as was shown by A. Cahn in his experiments on dogs. The organism saves its chlorine by checking its secretion. In spite of the diminished secretion, there may still be a great deal left in the system. In gastrosuccorrhœa, however, the conditions are altogether different. Through the constant irritation to the mucosa here, causing the excessive secretion of gastric juice, large quantities of chlorine are constantly withdrawn from the blood, and since they are removed from the body by vomiting or lavage, reabsorption is prevented, so that the body suffers an actual loss of chlorine. At the same time these patients do not take the proper amount of food, and, therefore, not the proper amount of chlorine to make up for the loss. In other words, there is increased excretion of chlorine, and the amount ingested is decreased—a unique pathological condition which must lead to an impoverishment of chlorides in the system. We may well assume that this diminution of chlorine plays some part in the development of tetany.

In looking through the literature I find that Korszynski and Jaworski as early as 1891 already regarded the decrease of chlorine in the tissues as the probable cause of gastric tetany. It is remarkable that this view can nowhere be found quoted in the text-books, in the special articles on gastric tetany by Fleiner, Albu, and others, or in Frankl-Hochwart's monograph "On Tetany," in Nothnagel's series. Yet their theory is of great assistance for the treatment of that peculiar and dangerous condition.

Korszynski and Jaworski, following their theory, recommended the injection of large quantities of normal salt solution, subcutaneously or by rectum, in order to overcome the chlorine starva-

tion in cases of gastric tetany.

Tetanic attacks are of serious import, and often lead quickly to a fatal issue. In the latest summary by Albu of these cases, forty in all, there were thirty-one deaths—i.e.,  $77\frac{1}{2}$  per cent. mortality. Their presence influences unfavorably the prognosis of an operation, and no operation should be undertaken in these cases before infusing large quantities of salt solution. This was done in our case before and after the operation, and it probably helped to bring about the favorable result, despite the presence of a perforation. To be sure, there were two other factors which favored the case: first, that the operation was performed only a few hours after the perforation; and, again, that the stomach had been washed shortly before the perforation occurred, thus preventing gastric contents from getting into the peritoneal cavity.

Albu claims that therapy offers no remedy which can either check or prevent a recurrence of the tetanic attacks. But, perhaps, as has been said before, it may be possible to end the attack by means of salt infusions. A recurrence can only be prevented by removing the cause. Their cause is, as we have seen above, motor insufficiency and the spastic or organic pyloric stenosis which hinders the passage of the more abundantly secreted hydrochloric acid into the intestines, thus preventing its reabsorption and depriving the system of large amounts of chlorine. In order to remove the cause the treatment should therefore be directed, first of all, against the motor disturbance. Whenever it is impossible to correct the motor insufficiency by internal means, it should be overcome by operation, either by pyloroplasty, gastroenterostomy, or resection, as the individual case may require. That is the rational treatment for gastrosuccorrhœa, as well as for tetany.

#### CHRONIC GASTRITIS DUE TO ALCOHOL.

BY NELLIS B. FOSTER, M.D., NEW YORK HOSPITAL.

In the large cities we are accustomed to see numerous cases of gastric disorders which can be traced directly to excessive and habitual use of alcoholic beverages. These maladies are very common in the low orders of society which make up the mass of hospital patients, and it was from this prominence of these affections that we became interested in them. It is, of course, well recognized that alcohol can produce a chronic gastritis, but the chinical differences of gastritis due to alcohol from gastritis of other causes is not at present so clear. At present we are concerned only with the secretory disturbances of the gastritis of alcohol. The methods of work were those ordinarily used in the routine examination of gastric contents, Ewald's test-breakfast of bread and unsweetened tea being given in the morning and expressed thirty minutes or an hour later. Free HCl was estimated by titration with  $\frac{n}{10}$  NaOH,

using dimethylamidoazobenzol and Günzborge reagent as an indicator, and phenolphthalein as an indicator in estimating the total acidity. Lactic acid was always tested for, as were the gastric enzymes.

The cases seen divide themselves into two classes: those presenting symptoms of gastritis and those without such symptoms. Of the first class but little need be said. The symptoms are familiar: nausea, with retching, on rising in the morning, and the vomiting, perhaps, of some mucus. These symptoms pass away after a couple

of "drinks" to settle his stomach; then he is able to eat his breakfast, and is free from discomfort until the next morning. The gastric motility in these cases is considerably accelerated. The test-meal must usually be removed after forty-five minutes, at longest, in order to recover sufficient material for analysis. There is much mucus present, both free and mixed with food. Free HCl is usually absent. Total acids are low. Pepsin and rennin normal. The following case may be given as typical:

CASE XXI.—Man, aged thirty-four years; clerk. Family history and past history unimportant. Habits: drinks considerable whiskey; always a glass before breakfast. For last month or two the patient thinks he has averaged about one quart of whiskey per diem.

Present Illness. Has felt run down for some time, but with no special symptoms, however, except morning vomiting for several weeks. Ankles swell slightly, and is puffy under the eyes in the morning. No pulmonary, cardiac, or urinary symptoms.

Physical Examination. Normal, except for slight swelling of

ankles. Urine: specific gravity 1024; no albumin or sugar; no

casts. .

Gastric Analysis. Ewald test-breakfast. Free HCl. 0; total acidity, 22; no lactic acid; enzymes present. Second analysis two

days later shows same results. .

The second class of these cases, those presenting no gastric symptoms, is of greater significance. The cases observed by the writer entered the hospital because of some malady other than gastric affections, and were recognized as possible cases of alcoholic gastritis on account of their habits or on account of the general alcoholic appearance. It was only after studying a number of the cases of chronic gastritis with pronounced symptoms that our curiosity was aroused concerning the gastric condition of those individuals who habitually use large amounts of alcoholic beverages, yet present no symptoms pointing to gastric disturbances. Hoping to obtain some light on this point, it has been our custom to make the routine gastric analysis on all of those cases that came into the hospital for any cause and whose appearance or history pointed to overindulgence in alcohol. The number of cases seen is now sufficiently large to permit of fairly accurate deductions. In contrast to the first class of cases there is no hyperkinesis, nor is there usually a great excess of mucus. The acid secretion being wherein morbidity is displayed, free HCl is always low, often absent, and in no case over 15. The average for our series is 5. The total acids are lowered, but not below the low normal limit. In other respects the gastric functions appear normal. The interest in these cases is mostly scientific, but there is, however, a practical application, namely, that one must be guarded in placing stress on the absence of free HCl in the diagnosis of stomach diseases unless free indulgence in alcohol can be excluded. The diagnosis of carcinoma

of the stomach in the early stages is based upon a number of small data, the most significant of which is, perhaps, the continued absence of free HCl. The point to which the writer wishes to call attention is that in these cases of possible carcinoma without definite signs or symptoms a history of alcoholic habits casts great doubt on that diagnosis. A case of the kind may be cited:

G. W., male, aged forty-eight years, entered the hospital complaining of weakness, loss in weight, and indefinite and occasional distress in the epigastrium. History and physical examination pointed to no organic disease. Blood count, normal. Gastric analysis showed absence of free HCl (three analyses). No diagnosis could be made, and an exploratory operation was done, which disclosed a small tumor in the tail of the pancreas (possibly carcinoma); the stomach appeared normal. There appearing no cause for the absence of free HCl in the gastric analyses, the man was later questioned concerning his habits. He had always drunk two glasses of whiskey before breakfast, he stated, and occasionally a glass during the day.

Riegel, Ewald, and other observers have pointed out the relation of alcohol to chronic gastritis; we are able to find no references, however, to indicate that there is recognized a change in gastric secretion due to alcohol previous to the excitation of subjective symptoms. Such a change as we have described is not accurately a gastritis chronica because, while there is slight increase in the mucous secretion, it is not marked nor constant enough to bring the syndrome under that head. It is, however, the precursor of that condition; and its interest in differential diagnosis, we hope, will

lead some one to confirm our results.

### A DIFFERENTIAL\*STAINING OF THE BLOOD WITH SIMPLE SOLUTIONS.

BY WILLIAM PAGE HARLOW, M.D., of BOULDER, COLORADO.

For the past year and a half the writer has been practically in daily use of some one of the methyl-alcohol-eosin-methylene-blue blood stains (Jenner, May, Grünwald and Wright's), and has experienced trouble at different times in obtaining a methyl alcohol that would, with one of the above powders, give results as satisfactory as with previous batches. Neither are the ready-for-use fluids furnished by the chemists uniform and always satisfactory in result. He believes this experience to be a common one with hæmatologists and physicians who are doing any considerable amount of blood work. Therefore, it seems permissible to call attention to a method

giving a color picture similar to and recommended over the above because of:

1. The simple and less expensive solutions employed.

2. The easy technique and rapidity of staining.

3. The more uniform results obtained with stains and alcohols furnished from different manufactories and at different times.<sup>1</sup>

The solutions used are:

No. I. Eosin, 1 gram, in absolute methyl alcohol, 100 c.c.

No. II. Methylene blue, 1 gram; in absolute methyl alcohol, 100 c.c.

The procedure is:

1. A fresh-spread cover-glass (or slide) taken in the usual manner.

2. Dried in air only.

- 3. Preparation, held in self-closing cover-glass forceps, covered with as much eosin as it will readily hold without draining, allowing same to remain one minute.
- 4. Eosin rapidly decanted (shake off the surplus). Do not wash the spread in water, and do not allow it to become dry by evaporation.
- 5. The eosin moist specimen quickly covered with the methyleneblue solution, allowing to stand about one and one-quarter minutes (different blues require a few seconds more or less than this).<sup>2</sup>

6. Wash gently in ordinary pure water (best to wash or dip spread in a glass of water, rather than in a strongly running stream from tap)

7. Dry between layers of filter-paper and mount in balsam.<sup>3</sup> The microscopic differential color picture shown by this method

with the blood spread is as follows:

#### The Red Cells.

The hæmoglobin-holding cells, when normal, are a deep red, clean and evenly stained.

<sup>1</sup> The greater part of the work done by the writer was with Grübler's Pure French Eosin, the "B" Patent Methylene Blue, med. pur., and an absolute methyl Alcohol made by C. F. Kahlhaum, Berlin. Though recent experiments with other foreign-made stains, and an Eosin and a Methylene Bluc furnished by Bausch & Lomb, and absolute Methyl alcohols furnished by Merck & Co., Eberbach & Son, Ann Arbor; E. H. Sargent & Co., Chicago, and Hynson & Westcott, Baltimore, have given quite uniform and very satisfactory results.

It should be noted when the red blood cells are stained bluish that it is because of an understaining with the methylene blue, and that the cosin which is more or less loosely combined with the oxyphilic substances has not had sufficient time to neutralize the action of the methylene blue which has been added in excess. This variation in the time for counterstaining with the methylene blue has heen found to be hetween one and one quarter and two

minutes in all the combinations that I have tried.

<sup>3</sup> Spreads dried in air may be kept unfixed, back to hack, between folds of filter-paper for several months, and still give quite satisfactory staining results. A recent staining and examination of one-year-old unfixed spreads of malaria, lcukemia, and perniclous anæmia showed that the hæmoglobin-containing cell stained practically as well as when fresh—i. c., anæmia, and all grades of polychromasia, nuclei, and the punctate hasophilic granules of Grawitz are shown, as well as the malarial plasmodium. But in the colorless corpuscles the granules are not well differentiated, the nuclei, and hasophilic substances only, heing well brought out.

In the chloroses they are somewhat paler and show light to clear central areas.

In pernicious and other severe secondary anemias, all grades of polychromatophilia, from terra-cotta, yellowish-brown, and greenish-yellow to a cloudy blue or purple are shown.

Small basophilic granulations are sharply brought out, being blue to deep purple in color, and found in cells the cytoplasm of which

may show any grade of polychromatophilia.

The nuclei are deep blue, and, in the larger forms especially, the

chromatin threads are clearly brought out.

The plaques, both in and out of the cells, are stained a lavender to dirty purple (but for the better study of the plaques, the simple staining of the unfixed spread for fifteen to thirty seconds with the methylene-blue solution alone is recommended. This is also good for all basophilic substances).

In the malarial plasmodium the cytoplasm is stained a bright light blue; the chromatin a deeper blue to purple; the segment walls are nicely shown, and the pigment appears as black dots or ovals.<sup>1</sup>

#### The Leukocytes.

Of the colorless polymorphonuclear granulated corpuscles, the neutrophiles generally show three or more quite dark-blue nuclei. The cytoplasm, taking a reddish tinge, is thickly studded with small violet to reddish granules, the whole apparently closely limited, as though by a cell membrane.

The oxyphiles, in a thickly spread blood specimen, are smaller than the neutrophiles, but in a thinly spread film usually appear larger than the neutrophiles. The nuclei, when there are three or more, as is often the case, are of the size and shape and stain the same as the nuclei in the neutrophiles, but more frequently there are two nuclei, oval or biscuit shaped, lying well apart in the cell, which are larger and stain a paler blue than the neutrophiles. The cytoplasm has a red tinge, if any, and is more or less loosely studded with large, glistening, rose-red granules that do not seem to be closely restrained, some often overlying the nuclei, others being entirely without the normal limits of the cell (the so-called "explosive" action after the drawing of the blood).

The basophiles generally are a little smaller than the neutrophiles, but vary in size to as large as the oxyphiles. The nuclei are often hard to differentiate from the cytoplasm, both being stained a pale blue. In some cases the nuclei are stained a deeper blue than the cytoplasm, are irregular in shape, and often eccentrically placed. But the coarse, spherical granules, varying in size from that of a

<sup>&</sup>lt;sup>1</sup> The addition of one-half per cent. of sodlum carbonate or lithium bicarbonate to the methylene-blue solution will give a better stain for the malarial plasmodium, but other structures are stained a little more blue than with the simple solution.

neutrophile granule to as large as fat-droplets, some staining a deep blue to purple or almost black, are distinctive.

The mononuclear granulated corpuscles or myelocytes stain about the same as the polymorphonuclear cells, having the same kind of granules. The nucleus is generally at one side and is round or oval, often showing two or more clear dots; and sometimes a fine reticular chromatin may be noted.

The neutrophilic myelocyte is the largest of this class. Its nucleus is large, often taking up more than half the cell, and is generally eccentrically placed. The cytoplasm is closely filled

with violet-stained relatively small granules.

The oxyphilic myelocyte is a little smaller than the neutrophile. Its nucleus is stained a paler blue and generally shows little or no structure. The cytoplasm is of a reddish tinge, and the granules filling the same, sometimes partly overlying the nucleus, are large and quite uniform in size, and stain a glistening rose-red.

There appear to be two forms of the mononuclear cell, containing basophilic granules, though both may be of bone-marrow origin,

and one an earlier form of the other.

The basophilic myelocyte (undoubtedly properly so classified because it is a mononuclear cell with basophilic granules, and can be demonstrated in normal and pathological bone-marrow) is a little larger than a polymorphonuclear neutrophile. It has a deep-blue staining nucleus located a little to one side of the centre. The cytoplasm is stained a lighter blue and is fairly well filled with basophilic granules about the size of the neutrophilic granules; these are stained a deep but real blue.

The other form, the origin of which has been attributed to the tissues and spleen, and classified as a mast-cell, is round or more often oval in shape, varying greatly in size—i. e., from being but little larger than a red blood cell to as large as a neutrophilic myelocyte. The nucleus and cytoplasm are stained a pale blue and sometimes cannot be differentiated; others of these cells, however, will show a well-defined and cloudy to deep-blue staining, oval or lobulated nucleus. The cytoplasm is stained a pale, clear blue, and studded with deep blue to royal purple granules which differ somewhat in size and shape, but most of which are large and coarse, and oval, triangular, or cuboid in form.

#### The Non-granular Mononuclear Corpuscles.

The small lymphocyte is about the size of a red blood cell and stains in at least three different ways, under apparently normal

conditions, and in the same specimen.

With this staining method, in one form, we see a small, nearly round cell with a relatively large pale-blue staining nucleus which may show two or more pseudonucleoli and a small amount of

chromatin. The nucleus is apparently nearly surrounded by a crescent of cytoplasm which exhibits a band of reddish staining cytoplasm next to the nucleus, then outward from this a pale-blue shading to a dark-blue periphery, or the dark blue contiguous to the red.

In a second form this surrounding cytoplasm seems curled or pressed up around the nucleus, and we see a pale-blue nucleus sur-

rounded by a very narrow band of deep-staining cytoplasm.

In the third form the cytoplasm seems to almost or entirely surround and cover the nucleus, and we get the same-sized cell, darkblue staining, with nucleus usually not apparent; but often nodal thickenings of the cytoplasm give the appearance of granules.

In some cases of lymphatic lenkæmia, where there is a great proliferation of these small lymphocytes, we may see a majority of the cells with the nucleus staining a hazy blue and the cytoplasm

tinged with blue, or nearly clear.

The large lymphocytes are the size of or larger than a polymorphonuclear neutrophile. They have a larger nucleus and an absolutely and relatively larger amount of cytoplasm; otherwise the description of the first form of small lymphocyte will suffice, and in general they may be classed together.

The large mononuclears and transition forms may be considered together. They have a structureless light-bluc staining nucleus, round or more often oval or indented (as kidney shaped), and with a relatively large amount of cytoplasm, which often is not stained and is barely discernible. In this there may be vacuoles and nodal

thickenings, but no granules.

In a series of specimens lately examined, a number of cells that, with other staining methods, would have been classified as "large mononuclear" or "transition forms," showed the double coloring of the cytoplasm, and it seems quite probable that they are merely

other forms in the chain of the lymphocytes.

There remain to be noted a group of mononuclear cells, product of the bone-marrow, and being either by-products (dying) or young cells intermediary in stage between basic cells and the corpuscles of peripheral blood. These have been noted as marrow cells (mark-zellen), stem cells (stamm-zellen), an earlier form of the mark-zellen and stimulation or irritation forms (Reizungsformen). These can be well classified together under the head of marrow cells. These are round cells about the size of the polymorphonuclear neutrophile. They all react to basic dyes only. In the young forms a nucleus is not noted, but we see a round cell staining quite deeply blue, being darker at the periphery. In this cell is a rough protoplasm having a "ground-glass" appearance, often two or more nucleoli or areas appearing vacuolated; and perhaps some granuloid areas due to thickened cytoplasm. In later stages a nucleus staining a little deeper blue than the surrounding cyto-

plasm is seen, otherwise with the same appearance as in the first

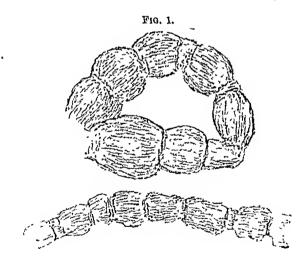
stage.

In still later stages the cytoplasm may begin to take on a violet or reddish hue, and granules begin to appear, when we must class the cell as a myelocyte. All grades between the diffuse-looking stamm-zellen and the fully granulated myelocyte may be noted.

# ON THE MECHANISM OF THE CONTRACTION OF VOLUNTARY MUSCLE OF THE FROG.

## By Edward B. Meigs, of Philadelphia.

As a first step in the search for a mechanical explanation of muscular contractility, it is necessary to have a definite idea of the change of form which takes place in a muscle fibre when it contracts. For various reasons I have used frog's voluntary muscle in nearly all of my experiments. It is well known that when a fresh frog's muscle is placed in distilled water it goes into a state



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Muscle fibres in water rigor.

of complete and lasting contraction called water rigor. If a muscle in water rigor be earefully teased, some of its fibres will generally be found in the condition shown by Fig. 1.

be found in the condition shown by Fig. 1.

Fig. 1 is a drawing of two fibres from a frog's sartorius in water rigor. The drawing was made with the camera lucida, and the outlines are, therefore, as true to nature as possible. The upper fibre

has been bent almost into a circle by the teasing, while the lower one is nearly straight. The specimen from which Fig. 1 was drawn was prepared as follows: The sartorius was dissected from the thigh of a freshly killed frog and placed in distilled water for about ten minutes. It was then carefully teased in a little water on a glass slide, the excess of water was removed, and a drop of glycerin applied. The preparation was then covered with a cover-glass, which was cemented to the slide with asphalt. The teased fibres were examined under the microscope in water before the glycerin was applied, and they were then seen to present the same appearance as in the drawing, except that the distended portions of the lower one were as symmetrically globular as those of the upper one in the drawing. I do not know why the glycerin caused the irregularity of outline of the lower fibre without affecting the upper one.

I have treated a number of muscles in the manner described and I have almost always been able to obtain some fibres from each muscle in the beaded condition illustrated; but in no case have I found more than a small proportion of the fibres of a muscle in this state. The following, however, will show that the beaded is the

true form of contracted muscle.

It is universally acknowledged that the contraction of muscle under electrical stimulation is the same as the normal contraction, and, therefore, if fibres can be shown to take the form of Fig. 1 when they contract under electrical stimulation, it must be admitted that the beaded form is the normal state of contracted muscle. It is not easy to observe beneath the microscope the change of form which frog's muscle fibres undergo during contraction due to electrical stimulation. If the muscle is large enough to be dissected out without damage, it is too large to allow its fibres to be seen clearly through the microscope. On the other hand, the least roughness in handling a small muscle destroys the irritability of all or of nearly all of its fibres. Besides this, the change from the uncontracted to the contracted form is so rapid that it throws the fibres under observation out of focus, and the contraction lasts at most only a few seconds, affording little time to get them in focus again.

I have found the sartorins to be the best muscle for this experiment. It is thin and flat and its fibres are parallel. If this muscle be carefully dissected from the thigh of a small frog and laid across the electrodes so that it can be observed through the microscope, the straight outlines of the fibres and the cross-striations can be distinctly seen. If now the tetanizing current be applied, the fibres will probably fly out of focus. But if they are quickly brought back into focus, it will be seen that their outlines are no longer straight,

but that they have taken the beaded form.

After a muscle lying on a pair of electrodes with its ends unattached has been thrown into tetanus, it never again completely relaxes,

but remains shorter and wider. This can be distinctly seen if the muscle be watched with the naked eye, and the fact is a great help in the observation of contraction. For, after the first application of the tetanizing current, the fibres, being already partially contracted, move to a much less extent with each subsequent application, and remain in focus, provided the objective used be of reasonably low power. If the tetanizing current be weak, and if it be applied for only short periods, the fibres may be seen with the microscope to contract and relax again and again, and the beading of the fibres can be seen to increase when the current is applied, and to diminish when it is removed. Of course, this beading of the fibres under electrical stimulation can only be seen at the cost of a good deal of care and trouble. I have again and again been disappointed by finding that the irritability of the fibres under observation has been completely lost; but I have repeatedly observed the increase and diminution of the beading on application and removal of the tetanizing current, and I have never seen a mere broadening of the fibres on application of the current and a narrowing on its removal.

It must be said, in passing, that the constrictions and bulgings of the contracted fibres cannot be regarded as "waves of contraction." As the bulgings do not entirely disappear on removal of the tetanizing current, it can easily be seen that they always occur at the same points. This seems to show that they are caused by definite structural peculiarities of the fibre. Moreover, the bulgings remain stationary during the flow of the current. It is impossible to conceive a stationary wave of any sort, and equally impossible to believe that "waves of contraction" could be present during tetanus, which is a state of complete contraction throughout the length of a muscle

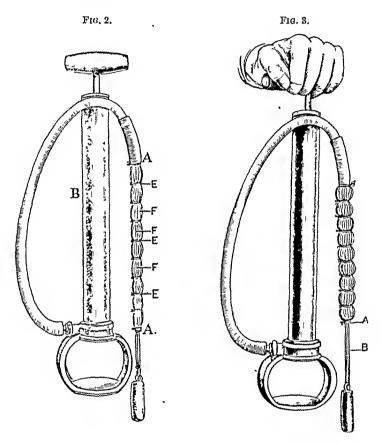
fibre.

It is, of course, difficult to observe the finer peculiarities of muscle fibres in tetanus. A whole muscle is an unsatisfactory object for microscopic examination, and the tetanus can last but a few seconds at most. As far as I have been able to discover, however, the appearance of fibres in tetanus is similar to that of the beaded fibres illustrated by Fig. 1. The important points of similarity are the disappearance of the cross-striæ and the great distance between the contiguous constrictions. The portion of a muscle fibre between two contiguous constrictions evidently contains many cross-striations, for the distance between two contiguous striæ is not more than a tenth of the diameter of the muscle fibre, whereas the distance between two constrictions is nearly equal to the diameter of the contracted fibre at its widest part.

It may be that observations similar to mine have been already recorded, but I have examined a good deal of the literature of the subject and have not been able to find any reference to the fact that frog's voluntary muscle fibres take the beaded form when

they contract. Ranvier, however, mentions the fact that the fibrils of insects' wing muscles often present the beaded appearance. But whether the facts have been recorded or not, they demand more consideration than they have hitherto received.

I shall now give what seems to me the most probable explanation of contraction. It is based partly on the observations recorded above, but the correctness of the observations is not affected by the probability or improbability of the explanation. I shall begin by showing that if the muscle fibre be assumed to have a certain mechanical



Fibre model.

Fibre model contracted.

structure, the phenomena of water rigor may be explained on perfectly well-known mechanical and physical principles. I can best describe the structure by exhibiting drawings of a model.

Fig. 2 represents a model supposed to have the structure of a muscle fibre. AA is a tube of thin rubber, encircled at intervals by wire rings, EEE. Along the tube run inelastic cotton threads, FFF, each of which is attached to all of the wire rings. B is an

<sup>1</sup> Leçons d'anatomie générale sur le système musculaire.

air-pump, by which air can be forced into the tube AA. When this is done the model takes the form shown by Fig. 3. Each of the divisions of the tube between the wire rings tends to become spherical, the cotton threads are thrown into curves, and, as they are nearly inclastic, the whole structure necessarily shortens. The illustrations are reproduced from photographs of the model taken at equal distances from it, so that the relative dimensions are preserved; the distance between the lines A and B (Fig. 3) represents the amount of the shortening.

It will be necessary now to return a step and consider what are the most obvious changes that take place when a fresh frog's muscle is placed in distilled water. These changes may be summed up as follows: The muscle absorbs water, it contracts, and its fibres change from the cylindrical to the beaded form. It may be proved that the muscle absorbs water by weighing it before placing it in the water and afterward. It will be found to be heavier afterward. The contraction of the muscle is remarkable in several ways. It is very slow, for about fifteen minutes elapse before it is complete; it is almost exactly equal to the greatest contraction that can be obtained with the tetanizing current; and once complete it lasts indefinitely.

The absorption of water by the muscle may be explained by the laws of osmosis. The shortening of the fibres and their change of form are immediately explained if they are supposed to have a structure mechanically equivalent to that of the model. For if they had this structure, the water passing into them by the osmotic process would compel them to change from the uncontracted cylindrical form to the contracted beaded form, exactly as air forced into the model compels it to change from the form shown by Fig. 2 to the form shown by Fig. 3. When the osmotic process is complete there is no tendency for it to reverse itself, and the muscle therefore remains contracted for an indefinite time.

There is one mechanical fact which greatly strengthens the argument. It is a necessary part of the construction of the model that the distance between the wire rings should bear the same relation to the diameter of the tube as shown by Fig. 2. Suppose that all of the wire rings except those at the top and at the bottom of the tube were removed, and that the threads and the rest of the machine were left as before, a much greater amount of air would then have to be forced into the tube before the curvature of the threads and consequent shortening of the model was as great as in Fig. 2; for the whole tube would tend to take the form of a sphere, and before it could assume this shape the rubber at the middle would have to stretch enormously, and the diameter at that point would be very great. On the other hand, practically no shortening can be produced in a machine with its rings much nearer together than those of the model (Figs. 2 and 3). It is a striking coincidence that the constrictions of the fibres in Fig. 1, the constrictions of frog's fibres in electrical tetanus, and those of the fibrils of insects' wing muscles are all at just such distances that the greatest amount of shortening can be obtained with the least expansion in volume and with the least stretching of the fibre sheath.

The four preceding paragraphs may be summed up as follows: All of the phenomena of water rigor may be explained on perfectly well-known mechanical and physical principles, if it be assumed that the muscle fibre has the same structure as the model shown by Figs. 2 and 3. It is known that water passes into the fibres by osmosis while the muscle is going into water rigor, and if the fibres have the structure in question, this passage of water into them is sufficient to cause both the change of form and the shortening. As the phenomena of water rigor can be explained by so simple an assumption, I have thought it justifiable to make the assumption.

The fact that so few of the fibres of a muscle in water rigor can be found in the beaded condition is, of course, a strong counterargument, but it must be remembered that distilled water is a reagent extremely destructive to muscular tissue. If the antenna of a living fresh-water snail be cut off near its base it will immediately contract. If it be then examined under the microscope in a little water, constrictions and bulgings are seen, not unlike those of the contracted muscle fibres. After a quarter of an hour the constrictions become much shallower and fainter, although the total length of the organ remains unchanged; and after half an hour or an hour they completely disappear. It seems quite possible that the constrictions of the muscle fibres are acted upon by the water in the same way as those of the snail's antenna. When it is added that fibres in electrical tetanus invariably present the beaded appearance, the fact that many fibres from muscles in water rigor do not present that appearance becomes insignificant.

If my explanation of water rigor is correct, it suggests very important conclusions. The structure which I have attributed to the muscle fibre is a highly specialized one, and it is apparently designed for the purpose of producing contraction. Besides this, it evidently acts when a muscle is thrown into tetanus by the electrical current, for fibres in tetanus exhibit the beaded form. The conclusion is inevitable that the structure in question is part of the mechanism of contraction.

To produce contraction in a structure like the model, it is necessary to increase the volume of the contents. There are only two ways in which this increase could be accomplished in muscle fibres. Either the contents of the fibres might expand or fluid might pass into the fibres from without. If contraction were caused by an expansion of the contents of the muscle fibres, it would necessarily be accompanied by an increase in the volume of the muscle. But it is known that the volume of a muscle does not increase during

contraction, and it cannot, therefore, be supposed that contraction is due to the expansion of the contents of the muscle fibres. If, therefore, the muscle fibre contracts in the same manner as the model, it is necessary to suppose that its contraction is caused by the passage of fluid into it from without.

It is thus seen that a consideration of the phenomena of water rigor and of the change of form which frog's muscle fibres undergo during contraction leads to the conclusions that the fibres have a certain mechanical structure which causes them to contract when the volume of their contents is increased, and that the ordinary contraction of muscle is caused by the passage of fluid from the spaces between the fibres into the fibres. (For convenience, I shall hereafter call the spaces between the fibres the interfibrous spaces.) It may be asked whether this conclusion in any way helps to explain muscular contraction. I believe that it does, for the passage of fluid from one part of an organ to another is a process which is quite likely to be explained on the principles of inorganic chemistry. There are several analogous processes, such as diffusion and osmosis. And besides this, the passage of fluid from one part of an organism to another is probably the most widely distributed and elementary process in the organic world. Plants universally receive their nourishment and grow by this process; it may be observed in the amæba during the extrusion of a pseudopod; and in the higher animals it takes place in the digestive tract, in the vascular system, in the kidneys, and in all of the glands. Not only this, but there is good reason to believe that this process is the cause of the movements of the insectivorous plants' and of Mimosa pudica.2

The points of similarity between muscles and glands have received some notice from physiologists. Rosenthal mentions these similarities in the work quoted above (see pp. 212 and 213). They are: first, the fact that both muscles and glands are thrown into action by stimulation of their nerves, and, second, certain likenesses in the electrical reactions. The following experiment seems to show a striking histological similarity. If one of the voluntary muscles be dissected from a freshly killed frog and immediately frozen and cut into thin transverse sections the sections present the appearance of Fig. 4, which was drawn from such a section with the camera

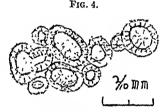
lucida.

The striking part of the appearance of Fig. 4 is the segmented ring of darker tissue which surrounds each of the fibres, and which resembles a layer of secreting cells. The fact that transverse sections of muscle prepared by the freezing process resemble sections of glandular tissue supports my hypothesis in the following manner: I have been endeavoring to show that the contraction of muscle is due to the passage of fluid from the interfibrous spaces into the

Charles Darwin. On Insectivorous Plants, London, 1875, second thousand, p. 255.
 I. Rosenthal. General Physiology of Muscles and Nerves, London, 1881, pp. 2 and 3.

fibres. The activity of a gland is secretion, which consists in the passage of fluid from the interacinous spaces into the acini, whence it is discharged through the ducts. In other words, according to my hypothesis, there is a fundamental likeness between the function of a muscle fibre and the function of a gland acinus. And if, in addition to this, there is a strong histological likeness between the two tissues, the fact constitutes a considerable addition to the argument.

The appearance of Fig. 4 can always be obtained by the following method: A frog is killed, the sartorious is dissected out, frozen, and cut into sections without being put in any reagent, and all this is done as quickly as possible. The sections may be floated out in a 0.6 per cent. sodium chloride solution or in distilled water and examined with the microscope. They will then be seen to



Cross-section of muscle prepared by the freezing process.

have the appearance of Fig. 4. Such sections may be preserved in glycerin. Alcohol produces a great decrease of the sharpness of the appearance. In very warm weather it is necessary to cool the frog with ice before killing it, and to dissect out the muscle and freeze it even more quickly than in cooler weather.

Whether the appearance presented by Fig. 4 or that of sections of muscles which have been preserved in alcohol or some other fixative, and have then been mounted by the paraffin or celloidin method, is more truly representative of the condition of frog's muscle during the life of the animal must be left to the judgment of scientific men. The answer to the question will depend on the answers given to two subordinate questions. First, Is the freezing process or is the alcohol and paraffin process likely to be more destructive? Second, Is the appearance of Fig. 4 or that of sections prepared by the alcohol and paraffin process more suggestive of mutilated tissue? In discussing the first question it must be said that frog's muscle may be frozen and melted again and immersed for a considerable period in 0.6 per cent. salt solution without losing its irritability.1 The process by which the appearance of Fig. 4 is obtained can be completed within ten minutes of the death of the animal from which the tissue is taken, and no reagent capable

<sup>&</sup>lt;sup>1</sup> American Text-book of Physiology, Philadelphia and London, 1901, 2d cd., vol. ii. pp. 58 and 162.

of destroying the irritability of the tissue is used. On the other hand, the alcohol and paraffin process requires many days for its completion, and any one of the reagents used is capable of destroy-

ing the life of the tissue.

It is difficult to discuss the question whether the appearance of Fig. 4 or that of alcohol and paraffin sections is more suggestive of mutilated tissue. Every histologist feels capable of judging from appearance alone which of two specimens of the same tissue is the more perfect, and yet it would be difficult for him to say on what he based his judgment. The distinctness of the outlines and the amount of differentiation in each of the specimens are, perhaps, the most important points to be considered. The sections illustrated by Fig. 4 certainly show more differentiation than the alcohol and paraffin sections. In Fig. 4 the fibres appear to be made up of two distinct parts, the central disk and the peripheral ring, and the latter is evidently divided into segments. In the alcohol sections each fibre appears as a nearly homogeneous disk. It is easy to imagine that the mutilation of a tissue whose true appearance was that of Fig. 4 might produce the appearance of the alcohol sections; but difficult to suppose that the mutilation of a tissue whose true appearance was that of the alcohol sections might produce the appearance of Fig. 4.

There is one difficulty which must be briefly considered before the conclusion of this discussion, namely, that the action of muscle is extremely rapid, whereas the process of the absorption of fluid is commonly regarded as a slow one. But the unusual conditions under which absorption takes place in muscle must be kept in view. The largest muscle fibres are in reality the merest threads, each of them is entirely surrounded by fluid, and there is, therefore, in every muscle a very large surface exposed by the fibres in comparison to the small amount of fluid to be absorbed by them. The finest cotton thread is exceedingly thick in comparison with even the largest frog's muscle fibre, and yet a cotton thread cannot be dipped in water for a fraction of a second without becoming saturated. The saturated thread has absorbed at least half its volume of water, and this is much more proportionally than would be required to cause complete contraction in a muscle fibre with the structure of the model. But a stronger argument can be adduced against the assumption that the contraction of muscle cannot be due to the movement of fluids because the fluids cannot be conceived to move sufficiently rapidly. If nothing further be conceded regarding the constitution of muscle than that it is composed of solids and fluids, it must be admitted that the fluids move whenever the muscle contracts; and the fluids could surely be moved by chemical processes as rapidly as by the movement of the solid parts of the muscle.

If I knew nothing further about muscle than that it was composed of solids and fluids and had the power of movement, it would

seem to me much more likely that the movement of the fluids caused the movement of the solids than that the movement of the solids caused the movement of the fluids. The former is the case in every machine made by man for the purpose of converting chemical into mechanical energy.

I realize that my conclusions are opposed to the latest results of scientific research, in so far as these seem to show that muscle fibres are composed of fibrillæ. If frog's muscle fibres are composed of fibrillæ, which are independently capable of contraction, the whole of the foregoing argument falls to the ground. I hardly dare to urge my own observations against those of such an authority as Rollett, and yet everything that I have seen seems to me opposed to the view that the muscle fibres are composed of fibrillæ. The appearance of the cross-section of frog's muscle, of which a drawing has been submitted, goes to show that fibrillæ do not exist in frog's muscle; and the beaded appearance of contracted fibres, whatever construction may be put upon it, seems to favor the idea that the fibre is the contractile unit. It may be urged that most of the work which tends to prove the existence of fibrillæ has been done with other muscle than the voluntary muscle of the frog, and the evidence favoring the existence of fibrillæ in frog's muscle is very unsatisfactory. It depends on the appearance of the muscle and on certain results to be obtained from specimens hardened in alcohol. Leaving aside the argument that appearance alone can never be a very satisfactory indication of mechanical structure, it must be conceded that the exact appearance of the interior of a fresh frog's muscle fibre is not very accurately known. Great amplification must be used to see the details of the structure which are supposed to represent fibrillæ, and with a high power little more than the upper surface of a thick frog's fibre can be sharply seen. As for the fact that frog'sfibres may, after a long immersion in alcohol, be teased into much smaller fibrillæ, there is no evidence to show from which part of the fibre these fibrillæ come. They may be merely portions of the fibre sheath. And there is a good deal of direct evidence to show that the interior of fresh frog's muscle fibres is in a fluid or semifluid state.

Sir Michael Foster' mentions the classic instance of the nematode worm seen making its way through the centre of a fibre. And Rosenthal<sup>2</sup> says: "It can be shown that a muscle fibre when recently taken from the living animal must, in reality, be of a fluid, or, at least, of a semifluid nature. So that it is impossible to affirm that either the discoid or the fibrilloid structure actually exists in the muscle fibre itself; it must rather be assumed that both forms of structure are really the result of the application of reagents, which

M. Foster. Text-book of Physiology, London and New York, 1891, 5th ed., part i., p. 95.
 General Physiology of Muscles and Nerves, London, 1891, p. 14.

solidify the originally fluid mass and split it up in a longitudinal or transverse direction."

It will probably be a long time before an adequate comprehension of the mechanism of muscular contraction is attained, and it is not to be expected that the subject could be completely elucidated within the limits of a single paper. I have simply pointed out the explanation which, after a consideration of the various facts, would seem to be the most likely one.

#### OBSTRUCTION OF THE CENTRAL RETINAL ARTERY.

REPORT OF A CASE.

By WILLIAM T. SHOEMAKER, M.D., of philadelphia.

THE question of embolism versus thrombosis of the central retinal artery has for a great many years been discussed and argued until it might be said to be almost threadbare; and, curiously enough, many of the best observers have titled their cases embolism, while declaring their belief in probable thrombosis. That this question is still an unsettled one in medicine is sufficient apology for further contributions.

The following case I believe to be one of lateral thrombosis of the central artery of the retina. The evidence to be adduced, though not

conclusive, strongly favors such a diagnosis.

F. W., aged seventeen years, twister in a mill, came to the Eye Clinic of the German Hospital November 18, 1903, with history as follows: One week ago, while returning home from a matinee, she suffered a sudden attack of partial blindness in the left eye. was described as everything becoming black before O. S., except in the lower field, where vision remained. Subjectively she noticed that the top of the head of a person looked at was not seen. condition did not improve, but, on the contrary, she thinks became worse in the succeeding few days. The attack was neither preceded, accompanied, nor followed by vertigo, headache, or any physical discomfort whatever. An interesting event in the history of the attack which must be considered, though it is, perhaps, a little sensational, is the following: The play which she witnessed was an extravagant melodrama, in which the heroine, during the third act, became suddealy blind, and continued so until the end of the play, with dramatic effect. The patient was much impressed, and, as she expressed it, could not get the afflicted heroine out of her mind. While thinking of this accident, she had proceeded but three squares from the theatre when her own trouble commenced.

<sup>&</sup>lt;sup>1</sup> Read before the Ophthalmological Section, College of Physicians, December 15, 1903.

Her family history is good. Her father and mother are living and well. She is the third of eight children, the oldest twenty-one years, the youngest three years; all living and healthy, except the seventh, who died in infancy. Her personal history is good. She had scarlet fever, measles, and whooping-cough in childhood; she has never had rheumatism, has no intestinal nor digestive disturbance; shows no evidence of syphilis, congenital or acquired. She menstruated at thirteen and has done so normally since. Two years ago she had typhoid fever, and was probably quite ill. At the present time she is well developed, of good color, and apparently well balanced. She seems to be in no way neurotic. She experiences some shortness of breath after sudden exertion, such as running up stairs.

Dr. Henry F. Page examined her heart November 27th; in his report he states: "Patient well nourished, color good, mucous membranes normal in appearance. Radial pulse soft, receding, and slow. Pulse rate 63. Inspection of chest shows slight bulging of left side, due probably to a slight degree of lateral curvature. Apex-beat not visible, but determined normal by palpation and auscultation. Slight pulsation of vessels of the neck. Fine thrill felt over carotids. Soft; blowing, systolic murmur heard at aortic and pulmonary orifices transmitted to the carotids." As a result of his examination, he

believes the murmur present to be functional in character.

A complete analysis of the urine was made in the chemical laboratory of the Medical Department, University of Pennsylvania, by Dr. John M. Swan. It is not necessary to read the figures; suffice it to say that the patient has nephritis, and is eliminating much less nitrogen, sulphates, and phosphates than normal. The albumin is less than 0.025 per cent. by Esbach's method; the casts are hyaline

and very few in number. There is no sugar.

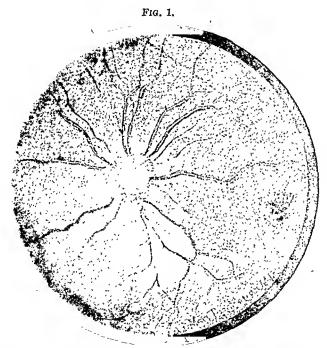
Upon admission, both eyes, conjunctiva slightly injected, pupils equal, irides freely active to light. Movements of eyeballs free in all directions. Central vision: O. S. (affected eye), 5/7.5. V.

O. D., 5/5.

Ophthalmoscopic Examination. O. S., media clear disk margins everywhere blurred, but more so below. There is a diffused area of ischemic infarction, mostly below, but especially marked in a localized patch about the size of the disk, situated 1 d. d. down and out. Into this patch runs an obliterated vessel from which has been a small extravasation. The lower temporal artery from its exit to a turn 1 d. d. from the disk is reduced to a thread; from there on it is of good size. A small branch from this artery running through the infarcted area is filiform, but peripherally recovers a normal diameter. Directly off the disk below are three small, indistinct, flame-shaped hemorrhages. Most of the arteries and veins are reduced in size; they all taper as they enter the disk, and many of them show a most irregular contour varying with diameters. The light streak on the smaller vessels is absent, and on the larger is diminished in

brilliancy, but continued far to the periphery. The light streak on a few of the upper ones is beaded. The vessels are nowhere tortuous, and peripherally they seem normal. The macular region shows a number of reflexes, streaked and radiating. The appearance here is granular, but there is no cherry-red spot. The porus opticus is enveloped in an impenetrable mist. Pressure on the eyeball causes a complete blanching of the disk, with not a vessel on the disk to be seen.

There is a little variation from the usual arrangement of the vessels. The majority of them, for instance, seem to come from the superior branch of the first bifurcation, there being at least seven from this source against three or four from the inferior branch. Among those



Obstruction of the central retinal artery. O.S., probably lateral thrombus.

first mentioned is a large artery running directly outward and curving above the macula, in close proximity thereto. This vessel, although it points to the lower retinal artery, probably belongs to the upper system because it passes above the macula and supplies the upper outer fundus.

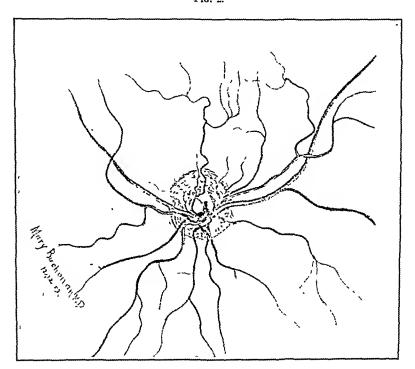
O. D. is normal ophthalmoscopically, but shows the same arrangement of the vessels. The upper fundus is much more vascular than the lower, and there is also a large macular artery, but in this eye it is a branch of the inferior system. There is in both eyes a tendency to lateral distribution of the vessels.

Dr. Buchanan, who has followed this case with me from the start, and who has been of great assistance in its preparation, has made

the water-color sketch, which shows well the condition about ten days after the attack. The rough sketch of O.D. shows the arrangement of the vessels in that eye.

Subsequent changes noted at intervals of two or three days have all been in the direction of increasing haziness of the retina (secondary ædema), enlargement of the veins and some increase in the diameter of the arteries. The small hemorrhages have disappeared. The infarcted area has become less pronounced by contrast. Vision gradually reduced until seven days after the first note it was 5/15. Since then it has improved, and at the present time it is 5/10.

FIG. 2.



Vascular arrangement of fundus. O. D.

November 25th. Two weeks after the attack a punctate deposit appeared on the posterior surface of the cornea, rather general in distribution, with a tendency to conical formation. This deposit has almost entirely disappeared. Fine vitreous opacities are now present. There has been no alteration in tension. The fields correspond to the fundus condition.

The clinical signs of thrombosis as given by Priestley Smith, in 1884 (Ophthalmic Review), and which might be said to have become classic, are:

(a) Previous attacks of transient blindness in the affected eye.

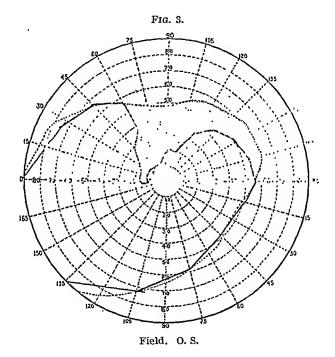
(b) Simultaneous attacks of transient blindness in the fellow-eye.

(c) Previous or subsequent attacks of transient blindness in the fellow-eye, especially if conditions of the attack were the same in the permanent as in the transient attacks.

(d) Signs of disturbance of the cerebral circulation at the onset

of the blindness-dizziness, faintness, headache.

In the history of the present case there are no points of correspondence with the above, but investigation along other lines would seem to make questionable the necessity for any one of these signs in establishing a case of thrombosis. It is true that with these clinical signs the case is probably thrombosis, but, with any or all absent, thrombosis is not to be excluded. In other words, when positive they are strong, and when negative they are weak. This case has been



studied therefore more from the side of general medicine and

general pathology than from the clinical.

There are three important causative factors in the coagulation of blood within the vessel wall during life, two or all of which are for the most part essential. These factors are alteration in the blood current; changes in the vessel wall, and alteration in the blood.

Ludwig Gutschy, in a recent article in the Beiträge for pathological anatomy and general pathology, has arrived at conclusions as to thrombus formation which seem to be of service in considering cases such as the one here reported. The first change he declares is one of separation; the fibrin separates from the blood plasma, forming a jelly-like mass, which adheres to the vessel wall, and

which he calls the *primary fibrin membrane*. Upon this membrane, which is sticky, leukocytes collect, the resulting mass being a white thrombus. T. Wharton Jones¹ has found that on pressing the neck over the artery or vein firmly with a blunt point, an agglomeration of colorless corpuscles, with a few red ones, held together apparently by coagulated fibrin, occurs, adheres to the wall of the vessel, and more or less completely obstructs it at that place.

Returning now to the three factors more or less essential for thrombosis; under the first, or alteration in the blood current, we have to consider anything which slows the blood current, such as weakness of the heart, narrowing of the bloodvessels, or pressure on the vessel wall. I think it can be demonstrated that the blood current in this case was very much reduced in velocity, especially in the central retinal artery. Normally the blood travels in the carotids from 300 mm. to 500 mm. per second, and in the very small arteries it travels but a few mm. per second.<sup>2</sup> The external diameter of the central retinal artery is about  $\frac{1}{10}$  mm.; it is therefore a very small artery, and has a very small lumen. Dr. Page's examination shows the pulse to be soft, receding, and slow, with a rate of 63 per minute. His examination was made under the usual conditions which tend to excite the patient and accelerate the heart-beat. If now the velocity of the blood in the radial artery is reduced below the normal to the extent shown by a pulse of 63, what must be the reduction in the central artery of the retina if we take as a standard Foster's figures just given? Furthermore, the axial stream in which the red cells travel is much quicker than the peripheral stream of plasma next the vessel wall. Here is certainly a condition favoring the separation of fibrin from the plasma, and the formation of Gutschy's primary fibrin membrane.

The next factor in thrombosis is alteration in the vessel wall. The patient has nephritis; it might, therefore, be said that she has endarteritis, arteriosclerosis, etc., but it is not likely, however, much as it would simplify things, if she had. Some change in the bloodvessel wall is very desirable for the purposes of this paper. This want is to be supplied by the bifurcation of the vessel. The point of bifurcation of the central artery of the retina—that point projecting in midstream, as it were—must necessarily stand more opposed to the onward flow of blood than the unobstructed wall. Such a mechanical arrangement causes a sudden halting of the stream with consequent embarrassment of some of the elements. Under these circumstances, and with an abnormally slowed current, the abovementioned changes of separation might well take place. This might also be favored by some individual peculiarity in the angle and form of bifurcation. This case shows peculiarities in the vessels of the

<sup>2</sup> Foster's Physiology.

fundus, and it is not unreasonable to think that the vessels are also. peculiar farther back. In support of this explanation is the experiment of Wharton Jones.

Changes in the blood itself have not been found. Two analyses were made by Dr. George P. Mueller, the second including an estimation of the fibrin. The first count gave: hæmoglobin, 100 per cent.; red cells, 4,650,000; white cells, 7650. Second count: hæmoglobin, 80 per cent.; red cells, 4,430,000; white cells, 5800. No increase in fibrin. Differential, normal.

This was somewhat of a disappointment as a functional heart murmur, which this undoubtedly was, is not usual with normal blood. My brother, Dr. Harvey Shoemaker, suggested that the blood quantity of the patient might be reduced as a whole. Cabot is authority for the existence of this condition. He has found it in typhoid fever, and attributes it to a concentration of the blood. There is no concentration of blood in this case, unless such concentration is offset by anæmia, for there is no increase of corpuscular

elements, the ratio remaining unchanged.

Clinically the case suggests the following points: From the changes observed in the fundus I would locate the obstruction laterally in the central artery near or at the bifurcation and passing into the lower branch. If the lower arterial system alone were involved, there should be no changes in the upper vessels other than those brought about by doing extra duty or carrying more blood. But they were changed in size, contour, and light streak. An embolus to produce this condition would have to be of that rare variety in which the plug straddles the bifurcation. That the macular region was not more affected is attributed to the peculiar arrangement of the vessels described above. The more normal condition of the vessels at the periphery, and the subsequent return of some of them to their normal calibre are changes described in many of the reported cases of obstruction, and in the absence of any opportunity for collateral circulation in this locality have been thought to be due to backward flow from loss of vis a tergo. The keratitis and vitreous opacities are inflammatory, natural results of this condition. The white area so characteristic in these cases, is pathologically infarction, and not cedema, as invariably called. Secondary ædema does occur, but I am told reaches only to the edge of the infarcted area. The process is one of starvation.

TREATMENT. For the general treatment of cases of retinal artery obstruction, it is important to determine, if possible, whether or not the obstruction is thrombosis. Against embolism we are helpless, and the other eye will suffer or not, as fate ordains. But if the conditions contributory to thrombosis, as above outlined, can be estab-

lished, they should be treated until they disappear.

Local treatment to be of any service must be immediate, and that these cases are sometimes seen early is shown by one of embolism which Dr. de Schweinitz had under observation twenty minutes after the attack.

Now, as to the immediate treatment of arterial obstruction in the eye, whether from embolism or from thrombosis, I am convinced that pressure massage, which has been strongly advised by most writers, is irrational and should not be practised. Pressure on the eyeball stops what flow of blood still exists, and produces the most favorable conditions for further agglutination and accretion. It tends to fortify the obstruction. Surely the indication is to increase the force of the circulation without causing vasoconstriction or to increase the heart action and dilate the peripheral circulation. The drugs of one class will do this, viz., the nitrites, and best among these are nitroglycerin and nitrite of amyl. These drugs cause rapid heart action and a dilated peripheral circulation. Gifford has recommended nitrite of amyl. The use of any vasomotor constrictor, which will cause the artery to contract and thus hold tighter the thrombus or embolus, is clearly out of place.

But better than any drug, it seems to me, would be forced muscular exertion, such as running or climbing stairs. In this way the heart could be accelerated, and the peripheral circulation, if affected at all, dilated. Had my patient been enough frightened to run home, I believe she would have been benefited.

Another therapeutic procedure which might be indicated in some cases, and probably was in this case, is hypodermoclysis, or the injection of large quantities of fluid into the cellular tissue of the body for the purpose of rapid absorption into the circulation. Likewise the intravenous injection of saline solution should constitute a part of our resources.

The prognosis of these cases is well known, and I have nothing to add.

# EMPYEMA OF FRONTAL SINUS, FOLLOWED BY EXTRADURAL ABSCESS AND ABSCESS OF FRONTAL LOBE; OPERATION AND DEATH FROM HYPOSTATIC CONGESTION OF THE LUNGS.

BY PAUL S. MERTINS, M.D.,

Abscess of the brain resulting from empyema of the frontal sinus is a sufficiently rare condition to demand the report of cases. The case which I here present is that of Mr. W. D. L., a boilermaker, aged about forty years, who came to the office of Dr. M. L. Wood, September 8, 1903. For the past six months or more he has suffered from violent headaches, which have steadily increased in severity.

Within the last three days a swelling, the size of a goose-cgg, has appeared in the region of the glabella. It was white, fluctuating, and very tender, and a harder rim, consisting probably of thickened periosteum, could be felt around its margin. On inquiry, a history of syphilis sixteen years ago was obtained. Two years ago he received a blow from a hammer on the top of his head, from which he was unconscious for several days.

The abscess was incised by Dr. Wood, and about one ounce of foul, dark-colored pus evacuated. The patient experienced complete and immediate relief of pain. He was instructed to go home, make hot applications to his head, and to return on the next day. On the third day the pain returned, and the patient noticed that when he held his head forward the flow of pus increased, and the pain became less. During the night of September 13th the pain grew more severe, the patient vomited several times, and had three convulsions. He was seen by Dr. Baker, who administered chloro-

form and morphine.

I saw Mr. L. on the following morning in company with Dr. Wood. He was in bed and seemed to be suffering greatly. His cerebration was slow, but relevant. No paralytic phenomena were observed. His pupils were small, equal in size, and reacted well. The eye movements were good in all directions. His breath was very foul, and the tongue, which was heavily coated, was protruded slowly in the centre line. His hand-grasp was strong, alike on both sides. His patellar reflexes were lively. No rigors have been noted. The ears were normal. The anterior end of the middle turbinate was greatly swollen. Temperature, 97.5° F.; pulse 78; respiration 20. His intimate friends stated that he has been considered stupid for a year or more, but his employer considered him an excellent workman.

On probing the wound necrosed bone was found, and in several places the probe seemed to enter the cranial cavity. A diagnosis of extradural abscess was made, and the patient was admitted to

St. Margaret's Hospital for operation.

Operation September 14, 1903, at 3.30 p.m., under chloroform narcosis, Drs. Wood, Baker, and Pollard assisting. I performed the following operation: A three-inch incision was made in the integument of the forehead, through the seat of the abscess. The pericranium, which had been dissected from the bone by the abscess, was held back by retractors, and an area of necrosed bone, the size of a silver dollar, was exposed. It was of dark-brown color, and presented the appearance of a pepper-box top, from the numerous fistulæ through which pus oozed at each respiration. A half-inch trephine was applied to the centre of the necrosed area and a button removed. An extradural abscess, containing about one ounce of pus, was found. The trephine opening was enlarged with rongeur forceps to the size of a dollar. The dura was found adherent to the frontal

bone all around, and formed the bed of the abscess. Removing the necrosed bone opened the left frontal sinus, and about one-half ounce of pus was found in it. The right frontal sinus on being opened was found to be healthy. The wound having been irrigated with a boracic-acid solution, the dura was examined. It appeared to be very thick, was of a dirty yellowish color, and pulsated only on the left side. No fistulæ could be found. A hollow needle was introduced on both sides, with negative result on the left side, but with the finding of four or five drops of pus on the right side as the needle was withdrawn. The needle was repeatedly reintroduced on the right side, but pus could not again be found. The wound was irrigated and an iodoform gauze dressing applied. The patient was sent to the ward at 4.45 P.M. in good condition. One-half grain of morphine was administered. During the night he became delirious, tore off the dressings, and was kept in bed by an attendant.

September 15th. The patient's general condition was good; his mind, though much clearer than before the operation, was not entirely clear. He was in a nervous condition, and picked at the dressing constantly. The wound was dressed. The right side of the brain did not pulsate. The patient complained of no pain. Iodide of potash, 10 grains thrice daily, to be increased to 30 grains, was ordered, in view of the history of syphilis. Bromide of potash, 20

grains every four hours, for nervousness.

The wound was dressed daily. His bowels were obstinately constipated, and cathartics were necessary to obtain a movement. His urine was frequently passed involuntarily. This condition of irritability and semistupor continued. On September 23d a transient paresis of the right internal rectus was noted, and examination of the eye-grounds showed an optic neuritis on the right side. On September 24th, as the patient seemed to be in a more than usually stupid condition, and was unable to answer questions, I decided

to aspirate the right frontal lobe again.

Second Operation. Drs. Wood and Baker were present. No anæsthetic was used. On introducing the aspirating-needle into the right frontal lobe at a depth of three-quarters of an inch, it was felt to enter a cavity and pus flowed into the aspirator. A small pair of scissors was entered by the side of the needle and the blades separated. About one and a half ounces of creamy pus and yellowish lump of broken-down brain tissue were evacuated. The cavity was gently curetted, and an iodoform gauze drain inserted. The patient's condition showed an immediate improvement. His mind became much clearer, and for the first time he spoke without a question being asked. His pulse rose from 78 to 100 beats per minute.

The accompanying chart gives the patient's pulse, respiration,

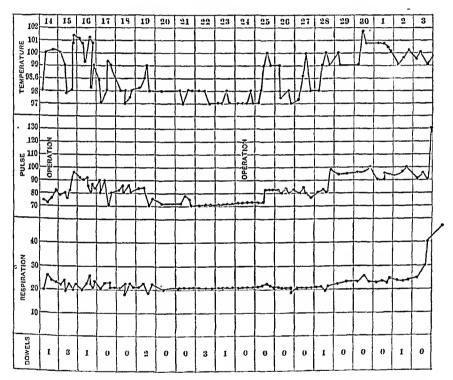
and temperature while in the hospital.

The patient's condition continued to improve slowly. The abscess

cavity grew smaller and the discharge less. Granulations began to cover over the exposed dura. His appetite continued good and his mind clear. The wound was dressed daily.

On the evening of September 30th I found a marked change in the patient's condition. His mind was less bright and his answers were much slower. His temperature was  $102^{\circ}$  F., pulse 98, and respiration 24. The wound was in good condition and draining freely. Examination of the chest showed a hypostatic congestion of the inferior lobe of the right lung; and the nurse informed me that during the afternoon the patient had coughed up several mouthfuls of blood. Strychnine  $\frac{1}{30}$  grain and brandy  $\frac{1}{2}$  ounce every four

FIG. 1.



hours was ordered, and directions were given to change the patient's position often. On October 3d the left lung became involved, and the patient's condition much worse. His urine and feces were passed involuntarily, and his pulse and temperature rose. His mind continued clear.

On the morning of October 4th he had a hemorrhage of several ounces. Morphine ½ grain was given, and an ice-bag was applied to the chest. He was unable to take his nourishment, and died on the morning of October 5th, twenty-one days after the operation, from exhaustion.

Autopsy fourteen hours after death. Drs. Wood, Hudson, Pitts, Billings, and William Thigpen were present. On removing the

sealp a depressed fracture, the size of a hammer-head, and about one-half inch deep, was found on the left parietal bone, near the sagittal suture. An opening the size of a match-head was found at the bottom of this depression. The bone was healthy, and this was probably the result of the blow received two years ago, from which he was unconscious for several days. On removing the calvarium the dura was found to be adherent around the original trephine opening, both to the bone and to the brain. It was also adherent to the bone at the point of the depressed fracture. The membranes appeared normal, and no increased amount of eerebrospinal fluid was noticed. The brain appeared normal, except at the point of operation, where an opening, 1 cm. in diameter, was

FIG. 2.



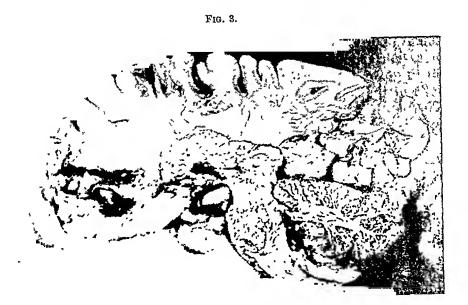
Photograph of brain, showing opening of abscess and adherent dura.

found leading into an abseess eavity. The longitudinal sinus was found normal: The brain was placed in a solution of formalin to harden. On opening the thorax the heart was found normal. Both inferior lobes of the lungs were found to be in a condition of hypostatic congestion, and on section of the right lung a cavity the size of a walnut, filled with clotted blood, was found. Old adhesions were found on the left side, between the pleura of the lung and diaphragm. The abdominal cavity was not opened.

The photographs of the hardened brain show the location and size of the abseess. In the photograph of the entire brain the dura has been left adherent to the brain about the abscess opening, showing that the abscess was well walled off. The opening into

the abscess is seen as a dark spot on the right side. The small rupture in the brain was made in removing the skull-cap. In the sagittal section the depth of the abscess, one and one-half inches, is seen. In this section the abscess was found to be well walled off by a thick lining membrane. The brain tissue about the abscess was in a nearly normal condition.

The dark area below the abscess is an extravasation of blood.



Anteroposterior section of brain, showing depth of abscess cavity, a part of lining membrane, and hemorrhagic focus below abscess.

Remarks. From the condition of the brain at autopsy, I think we have every reason to believe that this patient would have recovered from his abscess. The pulmonary complications were, without doubt, the cause of death. The abscess was the direct result of the empyema of the frontal sinus. The posterior wall of the sinus was necrosed and a fistulous tract was found from the sinus to the extradural abscess. This case is similar to that of Roth¹ in many respects; an external abscess was found, an extradural abscess and abscess of the left frontal lobe. His patient died. Macewen² reports a case of abscess of the frontal lobe with recovery. This case was, however, of traumatic origin. Professor G. Killian³ discusses three other cases of intracranial complications following empyema of the frontal sinus, namely, those of Carver,⁴ L. Müller,⁵ and E. Fraenkel.⁶

<sup>&</sup>lt;sup>1</sup> Wiener klinlsche Wochenschrift, 1899, No. 14, p. 383.

Pyogenic Diseases of the Brain and Spinal Cord.
 Archives of Otology, August and October, 1901.

<sup>&</sup>lt;sup>4</sup> British Medical Journal, June 16, 1883. <sup>5</sup> Wiener klinische Wochenschrift, 1895, p. 194.

<sup>6</sup> Virchow's Archly, vol. cxliii. p. 80.

## CHONDRODYSTROPHIA FŒTALIS.\*

By P. W. NATHAN, M.D., of New York.

THE majority of chondrodystrophic individuals are either born prematurely or born dead at term. The affection is, therefore, a very serious fetal disease, with a high mortality. Those infants which are born alive are usually very weak, and for some time life is precarious; should they, however, survive this critical period, they seem to grow stronger, and later they are no weaker than normal infants of the same age.

The nature of the affection thus accounts for the fact that up to the present time practically all the reports of cases have simply contained post-mortem findings. The earlier observers contented themselves with a description of the external characteristics; and these they found so closely analogous to those found in rachitic infants that they found no hesitation in classing the two conditions together. Thus the disease became known as an antenatal prototype of rachitis, being sometimes called congenital rachitis, sometimes fetal rachitis.

The earliest published case dates back as far as 1791, when Sömmering¹ reported his post-mortem findings of a case of fetal abnormality, which he did not attempt to classify. From his description, which is fairly accurate, there can be no doubt as to the nature of the condition. The bones are said to present the characteristic rachitic abnormalities; the fœtus is obese; the extremities are much too short, and much bent and deformed. In 1836 Busch² gave a very accurate description of a case, which he called congenital rachitis. He notes all the salient features which characterize these cases, viz., very large head; short, deformed extremities, with hard skeleton, large epiphyses, so-called rachitic rosary, rachitic pclvis, and general obesity. Following him numerous writers gave more or less accurate descriptions of cases which, in the light of our present knowledge, may be considered cases of chondrodystrophia fœtalis.

The majority of these writers, however, drew their conclusions as to the nature of the abnormality from the more or less cursory examination of a single case; and it was not possible, until the publication of the more extensive and careful observations of H. Mucller<sup>3</sup> (1860), to formulate a distinct and coherent idea of this singular affection. H. Mueller's researches, which are remarkable for their accuracy and insight, may be said to have formed the basis for all future investigation. He showed decisively that chondrodystrophia is a disease of the primordial bone cartilage; that it has nothing in

<sup>\*</sup> Read before the Orthopedic Section of the New York Academy of Medicine, Oct. 16, 1903.

common with rachitis, and that the inhibition of the growth of the long bones, which is the most prominent characteristic of the condition, is due to a disturbance in the row formation of the proliferating cartilage cells. The examples which he first examined occurred in calves, but he re-examined the cases previously published by Virchow as congenital rachitis and congenital cretinism, and found that in man the pathological phenomena are identical.

Some time afterward (1873) Urtel carefully examined a stillborn child macroscopically and microscopically, and his findings were identical with those of Mueller in the principal features; he hesitates, however, to place his case in the same category, because they differ in some particulars. Later investigation has proved his

hesitation unwarranted.

The further development of our knowledge of chondrodystrophia feetalis we owe to Eberth, Schidlowsky, Kirchberg, Marchand, but above all to Kaufmann, who, having special opportunities for investigation (he had thirteen cases), was enabled to clear up many

points in the pathology.

EXTERNAL APPEARANCE. The appearance of a chondrodystrophic fœtus is characteristic. The head is very large and appears still larger in contrast with deficient length of the fœtus as a whole. Both upper and lower extremities are too short. The arms do not reach the waist-line, and the lower extremities are so short that decentralization of the body is produced. Thus, the midpoint between the crown of the head and the soles is not, as it should be in normal infants, at the navel, but above it; in many cases as high as the xiphoid cartilage. The extremities, moreover, are bent and deformed, and occasionally fractured. All the epiphyses appear more or less enlarged, and those of the ribs produce the so-called rachitic rosary. The skin and subdermal tissues are hypertrophied, causing an exaggeration of the natural skin-folds; the abdomen is prominent, and the fœtus as a whole appears very obese. There is frequently epicanthus; the lips, eyelids, and tongue are thickened, and the latter protrudes from the mouth.

The anomalies of the skeleton give the fœtus that peculiar appearance which has long been known to be characteristic of rachitis, and which has led so many observers into the error of associating these two conditions. But aside from the pathological differences, which will be spoken of later, the peculiarity of the head and face in chondrodystrophia fœtalis should lead one to suspect that, similar as are the other external phenomena, these at least are peculiar to

another affection.

As has been pointed out, the head is abnormally large; indeed, it is so large that its circumference equals the length of the body, and in many cases exceeds it. The distinguishing characteristic, however, is the decided prognathus, with marked retraction of the nose, and, in some cases, flattening of the whole nasal region. The latter

abnormalities very much resemble those of infantile myxœdema, and where, as is usually the case, they are associated with thick lips, protruding hypertrophied tongue, epicanthus, and prominent abdomen, the resemblance to the congenital cretin is so close that without a microscopic examination of the bones, or a clinical history, the two conditions cannot be differentiated.

PATHOLOGICAL ANATOMY. Before proceeding to the discussion of the pathological changes at the base of the skull, a few words as

to its anatomy and development are necessary.

Upon the development of the base of the skull depend the peculiarities in the shape of the head and the physiognomy. Most important in this respect is that portion of the base of the skull which Virchow designated the os tribasilaris, and Hyrtle the fundamental bone. This bone is composed of the basilar process of the occipital bone, the os basilaris posterius, and the two portions of the body of the fetal sphenoid, the os basil. ant. and os basil. med. three parts of the compound bony os tribasilare are, in fetal life, separated by synchondroses, the synchondrosis intersphenoidalis and the synchondrosis spheno-occipitalis, which at birth are only partially ossified. Normally the synchondrosis intersphenoidalis is ossified at birth or soon thereafter; the synchondrosis spheno-occipitalis, however, remains patent until at least the thirteenth year, and complete synostosis occurs between the eighteenth and twentieth years. The growth of the base of the skull depends upon the persistence of these synchondroses; synostosis or even a disturbance in their development therefore produces a shortening of the base of the skull. As deficiency in the length of the base of the skull always causes prognathus, the relation of the above-mentioned synchondrosis to the prognathus is evident. In the case of so-called congenital cretinism, which Virchow used to demonstrate this fact, there was complete synostosis of the synchondroses os tribasilare, but he did not claim that synostosis was necessarily present in every case of prognathus. On the contrary, he laid particular stress upon the fact that not alone synostosis, but any deficiency in the length of the base of the skull would cause this anomaly. The writers following him, however, assumed that synostosis was the cause of prognathus in all cases; and this opinion was generally held, though the observations of Klebs,11 His,12 Marchand and Paltauf13 were opposed to such an assumption. In his examination of thirteen cases of chondrodystrophia Kaufmann was enabled to settle this question definitely; he found that not alone premature synostosis of the os tribasilare, but any inhibition of the growth of the os tribasilare or inhibition of the growth of any of the bones at the base of the skull causes prognathus. He found that synostosis of the os tribasilare was present in many cases of chondrodystrophia fœtalis, probably in the majority of them, but in a certain number the synchondroses are patent. Moreover, Kaufmann showed, by careful measurements of all the

bones at the base of the skull, that though the os tribasilare is a very important factor in its growth and development, it is not the only factor; for in some of his cases there was retraction of the root of the nose, though the os tribasilare was of the normal length. Even in those cases in which the os tribasilare is shortened or synostosed, it must not be assumed that this is the only part which is instrumental in causing the prognathus; not infrequently the bones anterior, the ethmoid, and nasal are also involved, either taking part in the shortening or, as occasionally happens, being entirely responsible for it (Kaufmann's Case XI.).

Another peculiarity of the base of the chondrodystrophic skull, first pointed out by Virchow, is a reduction in the angle formed at the junction of the basilar process of the occipital bone and the body of the sphenoid. Virchow called this condition kyphosis of the

saddle angle.\*

We must, therefore, conclude that the conditions which are active in causing the peculiar physiognomy in chondrodystrophia fœtalis vary within rather wide limits. They may be enumerated as follows:

1. Most frequent is premature synostosis, and consequently inhibition of the growth of the os tribasilare, with or without shortening of the bones anterior.

2. Shortening of the os tribasilare, patent synchondroses, varying degree of shortening of the bones anterior.

3. Decided shortening of the ethmoid and nasal bones, with slight or no shortening of the os tribasilare, and patent synchondroses. With these is associated a change in the saddle angle (kyphosis) of varying extent.

The bones of the skeleton present a variety of changes. They are always shortened and apparently thickened. In only a small percentage of cases, however, are the bones really thickened; as a rule, the apparent increase in thickness is due to the shortening, which changes the ratio between the length and thickness. The same is true of the epiphyses, which always appear larger than normal, though they are really enlarged in only a certain percentage of cases. In some cases, however, the epiphyses are enormously enlarged.

Sections of the long bones show that the pathological change occurs primarily in the growing cartilage. This portion of the bone, though it shows a variety of changes, is invariably affected in every case. The vascularity is always increased, but its size and consistency vary in different instances. According to the latter, Kaufmann distinguishes three distinct types: First, the epiphysis is not enlarged and the consistency is normal; second, it is absolutely enlarged, and the consistency may or may not be changed; third, the cartilage is softened.

The microscopic examination of the bones shows changes in the growing cartilage which correspond to the gross changes just enu-

<sup>\*</sup> Normally the saddle angle increases from the third fetal month until birth, when it is 155°; thence it diminishes to puberty.

merated. There is, however, one change which is constant and characteristic. This is the more or less complete inhibition of the normal row formation of the proliferating cartilage cells in the preparatory stage of ossification. The limitation of row formation is not, however, the same in all cases; though it is never absolute, in some cases it is almost so, and there is only a suggestion of row building in isolated areas of the ossifying zone. On the other hand, there are others which may, with propriety, be called mild cases, in which the row formation occurs, though the rows are stunted and rudimentary, inconstant, and irregular. Between these two extremes all gradations occur.

In the class of cases referred to as type one, which shows no increase, but rather a diminution in the size of the epiphyseal cartilages, besides the limitation in the row formation, there is also an inhibition of the proliferation of the cartilage cells. For this reason Kaufmann designates this type of cases chondrodystrophia fœtalis hypoplastica. In contrast to these is type two; here, though the row formation is rudimentary, the cartilage cells, instead of showing defective proliferation, are, on the contrary, enormously increased in numbers, and very closely packed together, causing the characteristic enlargement of the epiphyseal cartilage. This type Kaufmann designates chondrodystrophia fœtalis hyperplastica. The intercellular substance of the cartilage other than increased vascularity shows no change in the two types of the disease just described; in the third type, however, this is also abnormal. Here the cartilage has softened, in the severer cases quite extensively so, and the epiphyses appear as more or less completely gelatinous and very vascular masses, with variable dimensions. The intercellular substance is distended and forms an irregular network, in which cells of varying size are irregularly distributed. These cases Kaufmann designates chondrodystrophia fœtalis malica.

Thus, according to Kaufmann, we have three distinct types of chondrodystrophia fœtalis, viz., chondrodystrophia fœtalis hypoplastica, chondrodystrophia fœtalis hyperplastica, and chondrodystrophia fœtalis malica. Between these three types the rudimentary row formation is the connecting link, for it occurs in all of them, and is, therefore, the most characteristic and uniform change. Moreover, it must not be supposed that the three types occur perfectly distinct as individual cases; all three types may be found in the same individual in the various epiphyses, though one type usually pre-

dominates in a given case.

These pathohistological changes occur in all the bones subject to enchondral ossification, and they readily account for the dwarfism of not alone the long bones of the skeleton, but also for the shortening of the base of the skull and the resultant cretin physiognomy. The variation in the intensity of the process and its modifications, evidently, cause the variation in the conditions found in the latter

region. Thus, the prognathus may be due to the hypoplastic, the hyperplastic, or the malic process; any one of which may affect the cartilaginous skull in its entirety or one or more of the primordial cartilages more than others. With the cessation of the row formation, further bone development becomes impossible, and, as a result, ossification takes place, which may or may not be complete, according to the severity of the pathological process. Hence we find all gradations, from complete synostosis of the primordial skull vertebræ (os tribasilare) to only slight shortening, with patent synchondroses. In the malic form of the disease the affected primordial cartilages are soft, the ossification centres are rudimentary or even absent, and in the severer cases growth ceases entirely.

Synostosis of the synchondroses os tribasilare is, therefore, not, as the earlier writers assumed, necessarily present in all cases of chondrodystrophia fœtalis. Nor is the os tribasilare shortened in every case; so that the absence of either or both of these conditions does not decide the doubt, if any exists, that we have chondrodystrophia fœtalis before us in a given instance. All the bones at the base of the skull, which develop from cartilage, must be measured, and should the diagnosis still remain doubtful, it can always be cleared up by the microscope.

Besides the disturbance in the proliferation cartilage cells, there are still other peculiarities of the chondrodystrophic skeleton revealed by the microscope. It is found that the deposition of the calcium salts, no matter how great the abnormalities in the cartilage, goes on in a perfectly normal manner; the line of calcification is always found to be fairly regular, and the formation of ostoid tissue and its ossification is typical. Still more remarkable, considering the gravity of the pathological process in the cartilage, is the fact that periosteal bone formation goes on in a perfectly normal manner. Not alone this, but all the bones or parts of them which are formed and ossified very early in fetal life, or directly from connective tissue, pursue their normal course of development and show no abnormality. Thus the clavicle was found to be normal in length and other respects in all the cases reported; so also the bones of the cranial vault and all other bones similarly developed. In the long bones the normal development and ossification of the periosteal bone stands out in sharp contrast to the short and defective enchondrium, and the change in the ratio of the row gives rise to the appearance of thickening, to which attention has been called.

A very remarkable and interesting phenomenon which occurs in a great many and at some point in the skeleton in all cases of chondrodystrophia is what the Germans call the periosteal lamella. This very peculiar formation, which was first described by Urtel as it occurred in a human fœtus, later by Eberth in the calf, and subsequently by nearly all authors on this subject, consists of a layer of connective tissue emanating from the periosteum, from which it

pushes its way between the epiphysis and diaphysis toward the axis of the bone. Thus the epiphysis and diaphysis are separated more or less completely from each other. The periosteal lamella, which for reasons which will appear later I shall call the periosteal inclusion, varies in extent in the different cases and in the various parts of the skeleton in the same case. In the majority of instances it begins in the periphery as a distinct band, but gradually diminishes in breadth toward the axis of the bone, where it disappears. It is often apparent macroscopically, forming a distinct wall at the epiphyseal line, but it varies to a considerable extent, and not infrequently is only visible with the aid of the microscope. The breadth and the depth from the periphery usually correspond, so that when it is narrow it only invades the bones for a short distance, leaving a considerable portion of the axis free.

Microscopically, it can be seen that the cartilage cells adjacent to the periosteum inclusion run parallel with it, and assume a spindle form. The intercellular substance of the cartilage is fibrillated, and thus the transition between the inclusion and the cartilage is very gradual, at times almost imperceptible. On the diaphyseal side the conditions are liable to some variation. In some instances the inclusion undergoes ossification, with the formation of true bone, in a manner exactly similar to that which occurs under the normal periosteum (Urtel, Hoess, Leberth, Bode, Sturp, and others). In others, as in Kaufmann's Case II., the inclusion is surrounded by cartilage on both sides.

The relatively greater production of periosteum, as compared with the enchondral growth, is considered by all authors as the underlying cause of the periosteal inclusion. The manner of its production, however, is subject to some difference of opinion. Some authors (Urtel, Hoess) consider it due to an invasion of the cartilage by a periosteal process, due to an active local proliferation of the periosteum; and Kaufmann considers his Case II., in which the inclusion is surrounded by cartilage on both sides, as demonstrative of such a manner of production. It is difficult; however, to understand why the periosteum should proliferate excessively in a given locality without assignable cause. Eberth's explanation seems more plausible; he believes that the inclusion is due to the overgrowth of the epiphysis beyond the peripheral diaphyseal line, causing an involution of the periosteum, which subsequently proliferates. Kirchberg and Marchand also attribute the cause to an involution of the periosteum, but they consider this involution due to a continued growth of the periosteum, without a corresponding increase in the length of the bone.

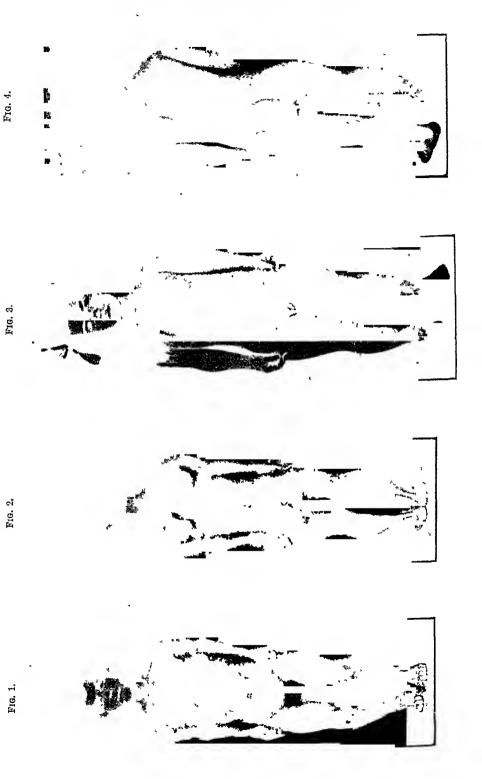
Personally, I believe that all these conditions, and not a single one alone, are, to some extent, responsible for the formation. I imagine the process of development to be somewhat as follows: The epiphysis enlarges until it grows beyond the peripheral diaphyseal

line, thus causing an involution of the periosteum at the point where the epiphysis and diaphysis join. Subsequently the diaphysis grows in thickness, but not in length, so that the fold of periosteum, instead of being eradicated (as it would be if the growth in length and thickness were in the normal ratio), becomes more pronounced, and is included between the adjacent surface of the epiphysis and diaphysis. The inclusion continues to act as periosteum; it therefore proliferates, forms ostoid tissue and true bone.

The periosteal inclusion, by its encroachment upon the epiphyseal line, necessarily precludes growth in length; and Kanfmann believes that this cessation of growth is analogous to that experimentally induced by injury or removal of the intermediate epiphyseal cartilage. But it must not be hastily decided that the cessation of growth is always absolute; in some cases the inclusion is very rudimentary, leaving a considerable portion of the axis of the bone free, and here the row formation, though defective, may still go on. It is only in those cases in which the periosteal inclusion is very extensive and undergoes ossification, thus causing synostosis of the epiphyseal synchondroses, that growth is definitely concluded. (Examples of such a condition occur in the os tribasilare and also, but less frequently, in the long bones.) Naturally, the earlier in fetal life the disease begins the more rudimentary is the row formation, the more complete the periosteal inclusion, and the more limited the growth

of the long bones. Thus, from an anatomical point of view, chondrodystrophia fœtalis is a well-defined morbid condition, and if we bear in mind its salient features, there can be no difficulty in differentiating it from other affections. The characteristic signs are defective growth of the enchondral skeleton, including the base of the skull and the pelvis, which, upon microscopic examination, is found to be due to the rudimentary row formation of the proliferating cartilage cells and the periosteal inclusion. In contrast to this is the normal ossification and the normal development of the periosteal and membranous bone. With postnatal rachitis it has absolutely nothing in common, except the apparent enlargement of the epiphyses, the prominent abdomen, and the occasional bowing of the legs; the latter is due to entirely different causes, which cannot be discussed here. Osteogenesis imperfecta, with which it has been confounded, differs from it in all the essential details. Here the salient pathological condition is a deficiency of ostoid tissue and defective ossification; the boncs are of normal length, and the skull and all the other morbid changes of chondrodystrophia feetalis are absent. Ostcoporosis and ostcosclerosis may both occur as complications of chondrodystrophia, but when present they are always secondary to the changes already described, and not pathognomouic.

Before closing our review of the pathology of this very interesting condition, though time presses, I cannot omit a few words as to the



pathogenesis. Mueller, Eberth, and a large number of authors consider the nature of this anomaly analogous to that of eongenital cretinism. However, though the skin and skull lesions lend some support to this view, clinical experience and the pathological anatomy teach us that the two diseases have nothing else in common. I think the changes in the skeleton and in the subdermal tissues point very distinctly to a constitutional anomaly, which, though not exactly analogous to that of congenital cretinism, nevertheless acts upon fetal organism in a similar manner; that is, by disturbing the metabolism in some unknown way.

CLINICAL ASPECT OF CHONDRODYSTROPHIA FŒTALIS. been said, the majority of infants with chondrodystrophia is born dead. But the disease is not nearly so uncommon as some authors would have us believe; and to judge by the number of living examples to be found in the literature, and my own experience, it is not necessarily fatal. Quite a number of isolated cases have been reported, and recently Kassowitz<sup>17</sup> has described seven cases which came under his own observation. I have had the opportunity to examine eight cases, a number of which I still have under observation. I have re-examined after an interval of several years (Case IV.); he was shown by Dr. C. Hermann, in the Pediatric Section of the Academy some time since. I show you his photograph, with that of Case V. Moreover, I have seen a number of adult cases walking about, and though I had no opportunity to examine them more closely, their appearance was so characteristic that I do not hesitate to elassify them. All my cases were seen within the last three years, and it is for this reason that I consider chondrodystrophia not nearly so uncommon as has been supposed; and I believe this statement will be borne out by general experience when the knowledge of this disease becomes more universal.

The general appearance of a chondrodystrophic infant differs very slightly from that of a fœtus with the same disease. They are dwarfs, with a large head, and very short, often bowed, extremities. In infants the abdomen is very prominent, as are the epiphyses, and there is obesity, but in the older cases these symptoms, though present, are not nearly so distinct. The head is large; in the younger individuals its circumference equals the length of the body in measurement, and there is a decided prognathus, which is accented by very marked retraction of the root of the nose, or flattening of the whole nasal region. The hair on the head is abundant, fine and soft, in my cases never coarse or brittle.

The lower extremities are always too short, being entirely out of proportion to the length of the trunk. This eauses a decentralization of the body and tends to give these individuals a very characteristic, at times ludicrous, appearance, and very readily distinguishes them from other dwarfs; for in cretinism, or in the so-called idiopathic dwarfism, the extremities and the trunk are both shortened and are

not out of proportion. The disproportion between the trunk and extremities in chondrodystrophia is readily demonstrated by measuring the height of the individual, first standing, then sitting. Measured in this way, my cases showed this peculiarity very distinctly:

					Height standing.	Height sitting.	
Case I.					. 21½ inches.	15½ inches.	
" II.	•		•		. 281/2 "	181/2 "	
" 1п.	•				. 23 "	143/4 "	
" IV.	•	•		•	. 45 "	291/8 "	
" V.	•				. 471/8 "	30 "	

The decentralization is also very well demonstrated by comparing the distance between the crown of the head and the umbilicus to that between the umbilicus and the sole of the foot. In the normal newborn infant these are the same, but as the child grows the distance between the umbilicus and the soles increases much more rapidly than the other, and exceeds it more and more as the individual grows older. In chondrodystrophia the midpoint of the body is not at the umbilicus at birth, but above it, sometimes as high up as the xiphoid cartilage, and this disproportion or decentralization of the body continues throughout life.

The upper extremities are also too short; they do not, as in the normal individual, reach to the hips. The fingers and toes are short, and, in fact, the conditions found in the living subject are exactly

what the pathological anatomy would lead us to expect.

During early life these individuals are obese, and the natural skin folds are exaggerated, but as they grow older the obesity gradually disappears. In all the cases I have examined, and as far as I can tell from the reports of other cases, the skin is never harsh and scaly, and the development of the hair on the head and other parts of the body is perfectly normal.

The mental faculties are always intact; these children are not sluggish and somnolent, but bright, taking an intense interest in their surroundings and learning to talk as readily as other children. If the older individuals are backward in their studies, it is more because they are apt to be kept from school because of their small size and peculiar appearance than from lack of intelligence. They begin to walk late, as a rule, and those cases with complicating ostcoporosis do not do so for a long time; but when they have learned to walk their gait is in no way peculiar or unsteady.

Like all infants with congenital abnormalities, they usually present some other congenital defects. The most frequent of these is inguinal hernia and a highly arched palate. In some of the postmortem findings dislocation of the hips is noted, but I have not been able to trace a direct causative relation between chondrodystrophia and the ordinary cases of congenital dislocation of the hip which we see in practice. Kassowitz attempts to bring them in connection, but I can hardly agree with him when he considers the fact that

patients with congenital dislocation of the hip are liable to other congenital malformations, such as epicanthus, highly arched palate, etc., as an indication of a connection between the two abnormalities. As I have pointed out, all individuals with one congenital malformation are very apt to have others. Moreover, I have carefully examined some twenty cases of congenital dislocation of the hip without being able to find any trace of chondrodystrophia. I must not, however, be understood to deny the possibility of the occurrence of dislocation of the hip in chondrodystrophia; I simply deny its causative relation to congenital dislocation of the hip in general.

Kassowitz also groups ehondrodystrophia with mongolism and myxœdema. In practice there is hardly any danger of confounding these affections. The mongols are idiots, without any disproportion of the skeleton, and with a characteristic mongolian physiognomy, which is absolutely distinct from that of ehondrodystrophia. Myxœdema is very readily distinguished from it; there is always mental defect; there are the skin and hair changes, and the disproportion between the extremities and the trunk is not present. That all three diseases have the abnormalities which are apt to appear in all congenitally abnormal individuals is certainly no reason for grouping them together, though Kassowitz very naïvely considers this a scientific classification. That this disease, like cretinism and some others, antenatal and postnatal, may be eaused by a disturbance of the metabolism can, in the light of our present knowledge of the normal metabolism, be neither positively affirmed nor denied. In chondrodystrophia the thyroid gland and the organs other than the skeleton show no change perceptible to us, and we must confess that the pathogenesis of this, as well as of nearly all other diseases, is still unexplained.

Of the etiology we know nothing. In one case a chondrodystrophic mother is said to have given birth to an infant similarly affected, but in all others we have nothing upon which to base a surmise as to the eause of this disease. To judge by the eases reported, the female is somewhat predisposed, though my own eases are equally divided between the two sexes.

MEASUREMENTS.
(Cases VI., VII., and VIII. were not accurately measured.)

	Case I.	Case II.	Case 111.	Case 1V.	Case V.
Age. Sex. Helght standing sitting Circumference of head Length from crown to umbilicus umbilicus to sole Ant. sup. spine to ankle Icmora Tribiæ Arms Forearms	16 mos. Male. 24¼ in. 15½ " 17½ " 7¼ in. R. 3½ in. L. 3¼ " 3½ " 3½ "	4½ yrs. Female. 28½ in. 18½ " 14½ " 14½ " 14½ " 16½ " R. 6½ "	9 mos. Malc. 23 in. 143/ " 175/ " 101/2 " 101/2 " 101/2 " 101/2 " R.141/8 "	14 yrs. Male. 45 in. 291/8 " 197/8 " 187/2 in. 107/4 "	14 yrs. Female. 47½ in. 30 " 21 " 26 " 20¾ "
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## LEUCONYCHIA STRIATA ARSENICALIS TRANSVERSUS.

#### WITH REPORT OF THREE CASES.

## By Charles J. Aldrich, M.D.,

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FIVE years ago at the Cleveland City Hospital, while examining a woman suffering from a very severe arsenical neuritis, I was struck by the observance of a peculiar white transverse line occupying the middle of the outer third of the finger-nails of each hand.

Taking into consideration the fact that the nails grow more rapidly following arsenical poisoning, I was able to estimate that these white lines corresponded to the time when, with suicidal intent, she had taken a teaspoonful of "Rough on Rats," which is well known to contain a large quantity of arsenic. The white streaks were about one-sixteenth of an inch in width, quite regular, with fairly sharp margins, and occupying an identical position on each nail. They were slightly larger on some nails than upon others and a little wider in the centre than near the margins; extended from side to side, forming a crescentic band, with the convexity directed to the free margins of the nail, and presenting a curve identical with that of the lunula. The markings were less plainly seen upon the toe-nails. Her body was covered with branny exfoliating dermal scales; much of the hair had fallen, and the palms and soles showed some kera-

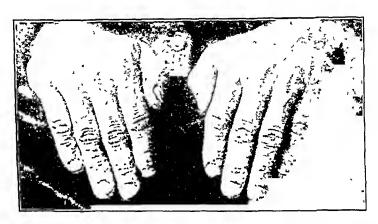
tosis. At that time I looked through the literature very earefully, but was unable to discover any reference whatever to such lines occurring in arsenieal poisoning, and while I felt positive that in my case they were eaused by the mineral, yet decided to wait for further confirmation of that opinion.

About twelve months following the observation of this case I was consulted by a man with an undoubted neuritis, who had been referred to me by Dr. F. W. McLean, of Elyria, and who gave the

following history:

He had suffered a very violent attack of "stomach difficulty" about three months preceding his visit to me. He says the vomiting was so violent that the vomitus contained blood. He did not suffer any marked eramps in the legs or arms. Shortly after he began to grow weak in his legs, and at last was barely able to get about with two canes.

Fig. 1.



On examination I found he was ataxic, had a partial double footdrop, absent knee-jerks, some loss of sensation, no pigmented spots or keratosis, no loss of sphineter control. In short, he had all the symptoms of a multiple neuritis. Inspection of his nails showed the characteristic transverse streaks as described, and as illustrated in this rather poor photograph (Fig. 1). It does not show the striation plainly. After talking with the patient some little time, during which he asked my opinion, I told him I thought he would probably recover from the neuritis, and that the neuritis was undoubtedly due to poisoning. At first he demurred, but after a little conversation told ine that he believed he had been poisoned, but offered no explanation except that he was positive that it was arsenieal poisoning. After urging upon him the necessity and the perfect safety of giving me his confidence, he confessed to having taken a large dose of white arsenie, but stated that it immediately produced vomiting, and ultimate recovery took place, save his nerve inflammation.

In May, 1899, Dr. George Gill, of North Ridgeville, Ohio, referred

to me a patient giving the following history:

F. S., male, white, aged twenty-nine years; has a wife and two healthy children. The wife is healthy; one induced miscarriage seven years ago. Patient gives a history of good health in early childhood; in early manhood gonorrhea, but no history of lues. I cannot learn that he has had any other sickness. He uses tobacco and drinks to excess. He states that one night about three mouths ago, on returning home from a debauch, he concealed a bottle of whiskey beside a hedge-row near his house. Becoming thirsty about 1 o'clock the next day he sought the bottle and took a large drink. In a short time he began to suffer extremely from pain in the stomach, vomited almost continuously, had cramps in the legs and arms, and became unconscious. His vomiting continued until 10 o'clock the following day. He remained in bed three days, and then got up, feeling very weak and still suffering from occasional attacks of vomiting and colicky pains in the abdomen. Six weeks later he began to feel tired, sore, and lame; the legs grew weak, the arms and hands felt heavy, weak, and numb. There was no loss of bladder power, but considerable diminution of sexual power. He unhesitatingly expressed to me the opinion that his nucle, with whom he had had trouble, had put poison in the whiskey.

Examination. Patient is a fair-sized man, walks with caues, gait ataxic; partial double foot-drop; station is not good, in fact, without his canes he is unable to stand with the eyes open. Both knce-jerks are absent, wrist-jerks and elbow-jerks are also absent. He is slightly anæsthetic throughout the lower limbs, which anæsthesia grows morc marked as the extremities are approached. He is proportionately more analgesic than anæsthetic. The fingers are slightly anæsthetic; he is unable to button his clothing well or to handle small objects. There is no tremor. The hand-grasps are equal and weak, registering thirty-six. There are no scars or spots on the body, and in fact nothing else abnormal is noted, except a white, slightly crescentic transverse streak on each finger-nail; the convexity of the crescent is directed toward the free margins. These streaks were so strikingly like those of the related cases that I immediately informed him that his stomach attack was due to arsenical poisoning. It was at this time he told me about the whiskey, adding that he thought his uncle had poisoned him. Shortly after this, in answer to some inquiries regarding the case, I received a communication from Dr. Gill, who informed me that the man had made a confession, which was corroborated by his wife, that he had taken a quantity of "Rough on Rats," with suicidal intent.

The accompanying black and white drawing (Fig. 2) affords an exact representation of the condition of his nails, and, indeed, the appearance common to each of the three cases observed. There were no transverse ridges on the nails, nor furrows; the lines were, in longitudinal relation at about the point which we would expect them to occupy from the outward growth of the nail since the poison-

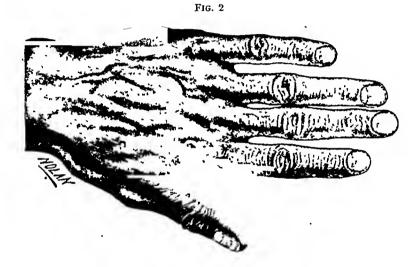
ing. His toe-nails also showed faint markings, but no keratosis was

present on the palms or soles.

I was about to publish these cases when I noticed the report of a case of arsenical neuritis by Dr. Florence Sabin, in the May number of the Johns Hopkins Hospital Bulletin, 1901, in which a white line running transversely across each finger-nail was referred to. In answer to a letter to Dr. Sabin, I received the following reply:

"Your note in regard to the white lines in the nails in cases of arsenical poisoning has interested me greatly. I do not know of any references in the literature, and Dr. Osler says that he does not. Dr. Osler expressed himself as anxious to see the photographs of

your cases."



Since the observation of a large number of cases of arsenical neuritis reported as occurring in beer-drinkers throughout England, and especially about Manchester, I have had considerable correspondence in reference to the condition of the nails with the English physicians observing those cases.

In April, 1901, Dr. Nathan Raw, of Manchester, wrote me that he had observed changes in the nails, particularly the toe-nails. He states that they were often markedly transversely ridged, but does not refer to any white lines. He very kindly sent to me the photo-

graph (Fig. 3).

Dr. Leslie Roberts, of Liverpool, writes me that he has not met with such changes herein described, and says, "Temporary arrest of nutrition and formation of air-cavities may produce various mark-

ings on the nails."

Dr. Ernest S. Reynolds, of Manchester, who was first to discover and point out the nature of arsenical poisoning due to beer-drinking in England, has very kindly written me under date of May 2, 1903, as follows:

"The white transverse streaks on the nails of cases of arsenical poisoning had already been noted and described by me. (See Lancet, January 19, 1901.) Also, you will there find an account of several parallel transverse streaks which I stated would almost suggest a series of drinking debauches.

"I am much obliged for your letter and much interested in it, as it corroborates my own observations. At the time a well-known skin specialist told me he did not think that the transverse streak had anything to do with the arsenical poisoning, but I observed it

too frequently for it to have been a mere coincidence."





Referring to Dr. Reynolds' article, which appeared in the Lancet, January 19, 1901, page 68, in the clinical description, and under the subhead "Nails," I find the following:

"In many cases the nails are affected. After the patients have stopped taking the beer for some weeks the best appearances are seen, for then there is a transverse white ridge across the nails; proximal to this the nail is normal, but distal to it the nail is whiter, cracked, thin, and toward the tip almost papery, and much flattened. In some cases there has been a series of parallel transverse ridges on the nails almost suggesting a series of week-end 'drinking bouts.' The deformed nails, of course, break easily."

It is to be observed that Dr. Reynolds speaks only of "a transverse white ridge." In my cases and also in Dr. Sabin's there was no welldefined groove or ridge. This difference is possibly due to the fact that his cases were subjected to more prolonged and chronic poisoning by the arsenic. I am nevertheless certain that they are both

evidences of arsenical poisoning.

It is possible that careful observation will show that these peculiar markings on the nails quite constantly follow severe acute arsenical poisoning, and I believe they depend upon the serious alteration in the nutrition incident to the profound shock of the poisoning, aided, perhaps, by the specific effect of the arsenic, since I have observed three cases of arsenical neuritis from slow poisoning in which there were no streaks, although the nails were ridged, particularly the toenails; nor did I observe in the cases of chronic poisoning that the nails were flecked with little white spots, which are vulgarly called "flowers" or "lies;" they were transversely ridged, pale, brittle, and papery. I do not believe that it is the profound nutritional disturbance alone which produces these transverse lines, since in neither of three cases of severe corrosive poisoning observed after seeing the first case of arsenical poisoning here recounted did white lines develop on the nails; nor has a diligent search through the literature revealed any observations of such changes in the nails following other severe poisoning. It is possible that the arsenic has some specific effect upon a plane of newly developed nail cells within the matrix, and as a result the normal keratinization fails to become physiologically complete.

If my contention is just we have in these nail-markings important corroborative evidence of poisoning by arsenic. The occurrence of these bands following arsenical poisoning is sufficiently established to warrant the use of the term leuconychia striata arsenicalis trans-

When I began a search of the literature for observations upon the nails it was with some surprise that I found that these transverse white lines had been observed, carefully described, and figured by several authors, but none, excepting Reynolds, ascribed them to One recorded case seems to show that they may appear as a congenital anomaly; other observations that they may present, as it were, an unguinal record of a severe illness.

While leuconychia punctata is frequently observed, one may obtain some idea of the rarity of leuconychia striata by the statement of Jules Heller, in his recent work on Diseases of the Nails, that it is so rare that but two cases have been thus far reported. justice to the literature, it is only right to state that Heller is afflicted with the usual literary myopia of German writers, as the following

references will evidence:

Reil,<sup>2</sup> in 1792, and Beau,<sup>3</sup> in 1846, published observations upon peculiar changes in the nails due to fevers; also Murchison, in his exhaustive treatise on fevers, alludes to these markings and changes

in growths.

Dr. Langdon Down observed two sets of white lines extending transversely over the nails on the fingers and toes of a man who had experienced two attacks of poor health, in each case the lines corresponded with the occurrence of the attack.

Prof. Alfred Vogel,<sup>5</sup> in 1870, and again in 1873, in thorough German fashion, discussed the question of nail changes following fevers, and figured several cases of the white transverse lines in the nails which appeared after typhus fever.

I found a description by Longstreth of transverse white bands extending over the surface of the nails, which appeared after each exacerbation of a case of relapsing fever, recording, as it were, each

relapse.

Da Costa' also has described such bands appearing after a relapse of typhoid fever, and gives a beautifully colored illustration of a hand the nails of which are traversed with several white bands, each corresponding to a relapse of the typhoid from which the patient had suffered.

Dr. Morrison,<sup>8</sup> of Baltimore, has described a case of transverse white bands on the nails, under the title of "Leucopathia Unguinum," occurring in an otherwise healthy young woman. There appeared a number of these white lines extending from one lateral nail margin to the other, and were about one-sixteenth of an inch apart. No cause for their origin could be ascertained.

Dr. E. J. Stout has reported a case where it appears that a negro

had presented such white bands on his nails from birth.

Heidingsfeld,<sup>10</sup> of Cincinnati, has contributed considerable to this subject in a very able article, "Leucopathia Unguinum." He has observed seven well-marked cases of leuconychia striata and nearly double the number of slighter degree. While he does not clearly state that all were due to injudicious use of the cuticle-knife, a "new and somewhat American instrument," I assume, in absence of any mention of other cause operative in his personally observed cases,

that each had its origin in tinkering vanity.

He is inclined to disagree with Heller and about all other writers upon the extreme rarity of leuconychia striata. His personal experience hardly warrants his contention, but rather convinces the reader that a very modern use of the cuticle-knife, a comparatively new and certainly vicious instrument, or an unskilful use of it in Cincinnati, is the explanation of his frequent observations. He has made some very interesting and valuable discoveries as to the pathological histology of these striations which seem to overturn the accepted theory of air infiltration. I give his conclusions in his brief recapitulation:

"Leuconychia is the result of some pathological change of structure of a plane of nail-cells, approximating a failure of the affected

cells to undergo normal physiological keratinization.

"The cause may be trauma, malnutrition, febrile diseases, neuroses, or any agency which disturbs the growth, development, or keratinization of the matrix cells in their change to nail-structure. "An infiltration of air is absent, and there is no rational physiolog-

ical basis for such a theory."

I have given these references to the literature at length for two reasons: First, to show that a thorough search reveals but little upon the subject; a few cases occurring in connection with fevers, some from traumatism; a very few of unexplained origin, and none ascribed to arsenic but by Reynolds. Secondly, as an aid to the diagnosis. Since, if in the presence of such nail changes as here described and illustrated we can exclude congenital anomalies, traumatism, severe illness, especially the acute specific fevers, particularly typhoid, relapsing and typhus, we will be warranted in suspecting arsenical poisoning. And if other corroborating evidences, such as violent unaccountable vomiting, abdominal pain, cramps in the legs and arms, and neuritis can be obtained, I believe we can positively assert that poisoning by arsenic has taken place. And allowing for the rapid growth of the nail following arsenical poisoning, and giving seven months for complete nail-growth, from the position of the white band, we can quite accurately estimate the time of the poisoning.

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# A CASE OF PRENATAL APPENDICITIS.

BY W. FRED. JACKSON, M.D., C.M.,

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This case, being of a very unusual nature, is presented as a contribution to our knowledge of this interesting and prevalent disease.

A female child, fully developed and well nourished, died at 5.30 P.M. from symptoms of metallic poisoning. At the hour of death the child had barely completed forty hours of natal life. At 12.30 P.M. the attending physician saw the infant, and it was perfectly well. Another physician was called hurriedly at 5.15 P.M. the same day, and found the infant collapsed and with a greenish-blue froth issuing from its mouth. This froth and accompanying fluid stained the garments a deep chemical blue. The supposition is that the child died of poisoning by the administration of a blue tablet of bichloride of mercury with citric acid.



A post-mortem examination, which I as Coroner ordered, brought to light the condition of the appendix, as shown in the accompanying illustration, which is taken from a photograph of the specimen.

The appendix is much elongated and congested, lying upon the cæcum, and bound down upon it by numerous and firm adhesions. The surfaces of the appendix, where it is reduplicated upon itself, are firmly bound together. The small intestine and the colon below the ileocæcal opening present no evidence of inflammatory action.

The mother's labor was regular and without incident. delivery was accomplished with the forceps without injury to the child. The infant was lusty and strong, and apparently perfectly well up to a very short time of its death. How the blue tablet was administered to the child, or by whom, has not been demonstrated.

It seems that the inflammatory condition, as evidenced by the thickened and congested appendix and firm adhesions, must have occurred previous to the child's birth. The more so, as the inflam-

mation was evidently in the stage of resolution.

# LUXATIO ERECTA.

# By George Tully Vaughan, M.D., of washington, d. c.

LUXATIO erecta, a variety of subglenoid dislocation, is so rare

that the following case is of interest:

J. M., white, male, aged sixty-six years, barkeeper, was admitted to Georgetown University Hospital October 4, 1903, having just been injured by being struck by a street car. On examination the patient's left elbow was seen pointing upward at an angle of forty-five degrees, the forearm was flexed, with the hand hanging down,

dorsal surface toward the patient's face.

The patient could not lower the elbow, even to a horizontal position, although the elbow could be moved inward toward the head to a vertical position without pain. The forearm was placed by me on the top of the patient's head, and the typical attitude of a case of luxation erecta was presented. The head of the humerus was easily felt low down in the axilla. Reduction was effected without trouble after about one minute's extension—seizing the arm with the right hand just above the flexed elbow and making extension upward and slightly outward, while the fingers of the left hand were used to press the head of the bone upward.

No anæsthetic was used and the manipulations were attended

with little or no pain.

The patient was last examined November 4, one month after the injury. He could abduct the arm well from the side and carry it across the chest, so as to place the fingers on the opposite shoulder. Flexion of the fingers was possible, but the grasp was quite feeble; extension of the fingers or of the wrist was impossible; there was well-marked "wrist-drop."

He said the fingers felt slightly numb, though rough tests with a pin indicated no difference in the two hands. Flexion and extension of the forearm and abduction and adduction of the arm were well

performed.

This variety of subglenoid dislocation of the shoulder was first reported in 1859 by Middeldorpf and Scharm, and up to 1899 Stimson had collected only 9 cases, which, with Middeldorpf's, made 11 cases in all. Of 539 shoulder dislocations observed at St. Thomas' Hospital no case of luxatio erecta was recorded (Makins).

Krönlein reports 3 cases of luxatio erecta in 207 dislocations.

In 400 dislocations Bardenheuer met with no case of luxatio erecta, but saw 2 cases in which the arm was abducted slightly beyond a right angle with the body—luxatio horizontalis—a variety of subclavicular dislocation.

# REVIEWS.

A Manual of Operative Surgery. By Sir Frederick Treves, Bart., K.C.V.O., C.B., LL.D., F.R.C.S. Second edition. Revised by the Author and Jonathan Hutchinson, Jr., F.R.C.S. 2 vols. Philadelphia and New York: Lea Brothers & Co.

In reviewing a new edition of a work so widely known and so deservedly esteemed as this, it is of chief interest to note the additions and omissions, the changes of opinion, or the confirmation of

earlier views wrought by ten years' experience.

In Chapter I. the most noteworthy change is the substitution in place of the remarks on "Cleanliness" of an article on the "Preparation of the Skin." There is perhaps no point in antiseptic technique as to which so much difference of opinion prevails as this, and the method described by the author, who prefers as the chief germicide a 1:500 alcoholic solution of mercuric potassium iodide, is not, so far as we know, employed in this country, and is worthy of trial.

In Chapter II. the chief addition is as to matters of *dress*. In this connection the author will probably be regarded by many American surgeons as unduly conservative, and only time and experience will show whether or not he is right. In the mean while his remarks will bring comfort to those operators who doubt the necessity of some of the elaborate precautions now fashionable.

Chapter III., on "The Operating Room," has been expanded and fully illustrated, and now includes a section on "Operations in a Private House," as to which the statement is made that "provided that the greatest care is exercised, there is no reason why as complete asepsis should not be secured in the patient's room as in

the most elaborately fitted hospital theatre."

This may be true, but as it is added that "it is in the first place essential that the house be in a perfectly sanitary condition, and as it appears to be an article of the householder's faith that the hygienic state of his or her premises is exceptionally perfect, it is well that the building should be examined by a skilled person without the residential bias;" and that it is desirable that "the room should be quiet, light, and well ventilated," that its windows look toward the south; that it should not be near a water-closet; should have an open fireplace, and should have as little gas burned in it as

possible, it is apparent that the author practically shares the widespread prejudice of surgeons in this country against operations in

private houses.

In Chapter IV., the directions for the sterilization of sponges by formaldehyde-misprinted "formal aldehyde"-would seem unnecessary in view of the almost universal preference—which the author

shares-for gauze pads.

The omission of the page devoted to an explanation of the abandonment of the steam spray marks one of the milestones in the advance of antiseptic technique. It seems now as if long before 1891—the date of the first edition—the "fort mit dem spray" of the German surgeons had been accepted everywhere.

In Chapter V. a little concession to "blunt dissection" is noticeable, and the teaching seems more in accord with the practice of to-day than the earlier and practically absolute prohibition of such

dissection.

On page 71 we note one of the few misprints that we have noticed,

viz., "gauge drain" for "gauze drain."

In Chapter VI. the most important addition is found in a paragraph which indicates a change in the methods of wound treatment, · and expresses unqualified preference for the practice of keeping the wound absolutely dry from beginning to end. "Micro-organisms cannot grow without moisture, and moist dressings and washing of the wound provide this medium." The details of treatment of an abdominal incision are given, and the author adds: "In my experience no method of dealing with wounds has given such uniformly successful results as this."

In Part II., dealing with the Ligature of Arteries, the previous inqualified opinion that "the best ligature material on the whole is chromicized catgut" has become: "There is considerable choice in the form of ligature used. . . . Kangaroo tendon, catgut, and soft silk of medium thickness may all be recommended."

The author's opinion in favor of the intraperitoneal ligation of the common iliac has been strengthened by further experience. He adds a quotation from Mr. Makins' article on that subject calling attention to the greater anatomical difficulties that surround the ligation of the left common iliac as compared with the operation

on the right side.

In Part III., as an addendum to the article on Meckel's ganglion, Mr. Hutchinson—the co-editor of this edition—says: "It is possible that an intracranial resection of the superior maxillary trunkperformed in a similar way to removal of the Gasserian ganglion -may prove to give more lasting results than the operations

The article on the Excision of the Gasserian ganglion has been much expanded and the positive statement that "excision of the gauglion by the temporal route is by far the best method, as it

offers a good prospect of permanent cure, and leaves hardly any deformity of the face," is fully justified by the experience of the last few years. The omission of Cushing's method is accounted for (apparently by the co-editor) with the statement that "it is largely a return to the old pterygoid route, involves division of the zygoma, and appears to have nothing to recommend it." Cushing's method is, however, not largely a return to the pterygoid route, and, in the opinion of many surgeons who have employed it, has very much to recommend it. The division of the zygoma is perhaps the least essential part of the method.

In the admirable section on Amputations the only addition to the statistics that we have noticed is a paragraph giving the result of ninety-four major amputations at the London Hospital from 1890 to 1900, with eleven deaths (Mr. Hutchinson). A wider survey of operative results in these cases during this important decade would, we believe, have been of interest and value, although this is not meant in criticism of the mortality (12 per cent.) in this series,

which is very creditable.

In the chapter on Interscapulothoracic Amputations no mention is made of the desirability, in some cases of malignant disease, of removing the entire clavicle instead of only the outer two-thirds (Le Conte).

In amputation of the leg the old term as to the "place of election" -a point "about a hand's breadth below the knee-joint"-is employed, although, in this country at least, the point of election has, with the improvement of prosthetic apparatus, descended at least to the junction of the lower and middle thirds of the tibia. No mention is made of an operation now in favor with many American surgeons, in which the tibia is sawn twice, so as to secure a periosteal flap without disturbing the relations of vessels, nerves, and muscles, and so as to prevent the adhesion of the latter to the bone and minimize bone atrophy. It is warmly recommended

(Matas, White) and has stood the test of experience.

In the section on Ununited Fracture it is correctly said that "as a practical measure the wire is a delusion and a snare, so far, certainly, as the long bones are concerned;" but when it is added that "the various forms of apparatus in which plates of metal are secured (outside the skin) to the fractured bone by long screws" are "equally fallacious and more dangerous," it would seem impossible to American surgeons that the author-or the co-editor-could be practically familiar with the ingenious Parkhill bone-clamp, here universally regarded as the best of all mechanical devices for securing fixation of the fragments of the long bones after resection of their ends in cases of non-union. The published results obtained in this country amply demonstrate both its safety and its utility.

Volume II. shows fewer alterations or additions. The excellent

section on Plastic Surgery remains largely unchanged.

We found no mention of intubation of the larynx in croup or diphtheria. The value of this procedure has been sufficiently demonstrated to justify its inclusion in a work of this comprehensive character, while it can scarcely be dismissed, as might catheterism, as

belonging rather to the field of minor surgery.

In describing the operations for hypospadias it would seem as though less space might be given to the elaborate description and illustration of Duplay's and Anger's operations, and more to the very excellent method of Wood, which is criticised, it would seem, on theoretical grounds, and not as a result of practical experience. In the writer's hands the preputial integument has yielded most satisfactory results when used to form the principal flap in this operation, and no trouble has been experienced with "edema of the lax subcutaneous layer."

A word of caution has been inserted in regard to the term "complete excision" in describing thyroidectomy, attention being called to the absolute necessity of leaving behind some portion of the

thyroid gland in all such operations.

In dealing with the surgical accident of the entrance of air into divided veins, the immediate treatment by filling the wound with fluid and expressing air from the chest by direct pressure is described, and the suggestion that air should be sucked out of the right auricle by a catheter passed into the heart is very properly spoken of as "preposterous." When, however, the author adds, "the advice given in nearly every text-book that artificial respiration should be resorted to is almost as silly; there is not too little air in the thorax, but too much," he does not seem to realize that the forcible compression of the thorax to expel the air is only a form of artificial respiration; that the pulmonary circulation must be re-established because otherwise the left heart remains collapsed from want of blood; and that artificial respiration offers the best means of meeting this tremendously urgent indication.

In the chapter on Abdominal Section a useful summary of the arterial supply of the abdominal wall has been added. The statement that the ileocæcal valve corresponds to the spinoumbilical line and that the root of the appendix will be placed more than one inch lower down, and perhaps internally to it, is of interest, but cannot be regarded as demonstrated by the researches of Dr. Keith, to which the writer alludes, and which at present lack confirmation, as does the further statement that the ileocæcal valve in a normal person is usually tender to pressure. The practical importance of the matter is obvious; there are reasons for believing that it is a fact and that it serves to explain some of the too frequent cases in which tenderness elicited by pressure in this region has constituted the chief indication for operation which has revealed a normal appendix.

In addition to the chapter on the Operative Treatment of Enlarged Prostate, the author—or the co-editor—says that castration

and vasectomy in this condition "have been practically abandoned." Mr. Reginald Harrison has reported 100 cases of vasectomy, in every one of which some degree of improvement resulted; and Rovsing, of Copenhagen, has recently (1902) reported 40 cases, of which 27 were cured, 9 relieved, and 4 unimproved. There were no deaths, and he adds, "I should, under no circumstances, feel myself justified in undertaking the total extirpation of the prostate in a patient in whom I had not done a vasectomy, which, in many cases, gives such extraordinary relief." The operations in question have certainly not yet reached their ultimate position in the estimation of the profession. It may be that they will be entirely discarded, but it would seem as though after the expiration of the inevitable period of indiscriminate employment of a novelty (of which Treves has himself complained in relation to the appendix) there would still be a restricted field of usefulness for them remaining; and that the statement that the operations are now practically abandoned is not fully borne out by the facts while men of the professional position of Harrison and Rovsing are still using them.

In the preliminary remarks upon operations on the kidney no mention is made of the two layers of the fat surrounding the kidney (Gerota), recognition of which is of practical value in approaching

that organ during an operation.

In describing abnormalities of the kidney, Mr. Morris' more recent figures have not been given; they would, for example, increase the cases of absence or extreme atrophy of one kidney from 1 in 4000 to 1 in 2400 cases. The remaining statistics on this subject are

similarly incorrect.

These are all, however, minor matters. The book, as a whole, has not yet been supplanted or replaced by any other single work on the subject in respect to the excellent average judgment that has been displayed in the difficult task of selecting from among thousands of varying procedures those most worthy of description, and in respect also to the simple, clear, straightforward manner in which the information thus gathered has been conveyed to the reader.

J. W. W.

THE PRINCIPLES AND PRACTICE OF SURGERY: DESIGNED FOR STUDENTS AND PRACTITIONERS. Lippincott's New Medical Series. By George Tully Vaughan, M.D., Assistant Surgeon-General, Public Health and Marine Hospital Service of the United States; Professor of the Principles and Practice of Surgery, Georgetown University. Philadelphia and London: J. B. Lippincott Co., 1903.

THE time has passed when it is possible for an author to present comprehensively in a small single volume the general surgery of

to-day, and yet there is a constant demand for such books on the part of the medical student and the man engaged in the general practice of medicine. It was with the idea of supplying this demand that the present work was prepared. It offers to the reader a condensed, and in most respects a thoroughly satisfactory, presentation of general surgery. The book is quite readable and comprehensive as far as possible in its limited space. It possesses, as such books always do, its points of weakness as well as its points of strength.

In our opinion the chapter on Anæsthetics is distinctly weak, since we feel that this is a subject so little taught in our medical schools that when the student turns to his text-book he should be able to find there all the necessary information regarding anæsthetics, and particularly as regards the method of their administration. The author speaks of bromide of ethyl as a general anæsthetic, although this agent is but little used at present, but he makes no mention whatever of chloride of ethyl, which is being so extensively employed for short operations and as a preliminary anæsthetic to ether. We think also that in the chapter on Fractures too little stress is laid upon the necessity of massage and movement, and particularly is this omission noticeable in the discussion of fractures of the lower end of the radius. We heartily approve of the author's teaching as regards the treatment of strangulated hernia, though we believe that, whenever possible in operating for this condition, a radical cure should be sought rather than the simple reduction of the hernia by the older methods of performing herniotomy. The chapters dealing with Genito-urinary Diseases are more complete than is usually found in single-volume text-books on general surgery.

A general criticism which we feel we must make of this work is the fact that the author has devoted too much space to the older methods of treatment and too little to recent and generally accepted methods, although it is possible that this is wiser in a work intended

chiefly for students and general practitioners.

The illustrations are many of them old, although there are also many reproductions of interesting photographs. G.

A Portfolio of Dermochromes. By Professor Jacobi, of Freiberg im Breslau. English adaptation of the text by J. J. Pringle, M.B., F.R.C.P., Physician to the Department for Diseases of the Skin at the Middlesex Hospital, London. London: Rebman, Limited, 1903.

The portraits in this atlas, as in a recent French one, have been made entirely after models, the great majority after those in Neisser's collection at Breslau, the remainder after models in the collections

of Lassar and Lesser, of Berlin; Hennig, of Vienna and Baretta, of Paris. A new color-printing process, called citochromy, has been employed in their production, for which is claimed absolute accuracy in the reproduction of colors. While the claim of absolute accuracy is hardly justified, the appearance of these-portraits indicates that the process is much in advance of any of those hitherto employed; we have rarely, if ever, seen more accurately colored pictures of diseases of the skin. The two parts of the atlas thus far published contain 78 portraits on 42 plates, the diseases represented being for the most part selected from among the commoner affections of the skin. The more important and interesting rarer diseases, however, are not omitted, there being excellent portraits of Raynaud's disease, actinomycosis, and anthrax.

Among the plates which especially deserve notice on account of their excellence are those representing various forms of psoriasis, particularly psoriasis gyrata, lupus vulgaris, lupus erythematosus, pityriasis rosea, pityriasis rubra pilaris, and the exanthemata. Two portraits, one representing variola, the other varicella in the adult, are very instructively placed side by side on the same plate. The portrait of scarlatina is most accurate in coloring, but measles is

not so successfully represented.

And just here seems the place to say that we have frequently woudered why portraits of the exanthemata do not find a place in every atlas of diseases of the skin, since in no class of affections do bluuders in diagnosis occur more frequently and result more disastrously.

As the atlas is not designed by its author to take the place of a text-book, the text is considerably condensed. The symptoms of the various diseases portrayed are succinctly and clearly given together with a brief outline of the diagnosis and treatment.

While portraits and models, however well made, can never altogether replace the study of the living subject, portraits as accurate in drawing and coloring as these make very efficient substitutes, and must prove of the greatest service in the recognition of diseases of the skin to those whose clinical opportunities are limited.

M. B. H.

A Text-book of Pathology. By Alfred Stengel, M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the Philadelphia Hospital; Physician to the Pennsylvania Hospital. Fourth edition, thoroughly revised. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

THAT pathology and clinical medicine are intimately related is shown by the fact that one so widely known as a clinician should be so widely read as a pathologist. The usefulness and popularity of this book, especially to the practitioner, is evident when one

considers that four editions have been called for within a period of five years. The book is so well known to pathologists in general that a detailed description is unnecessary. In the present edition numerous revisions and additions have been made, notably in the sections upon typhoid fever, tuberculosis, yellow fever, dysentery, and in the discussions upon diseases of the blood. A short account is given of the latest theories of immunity. In many places the results of the most recent researches in pathology are alluded to, but, as in the earlier editions, references are intentionally omitted. A very wide range of subjects is dealt with and throughout the book special attention has been paid to physiological pathology. In this respect and in many other ways the book is essentially a clinical pathology. An appendix has been added in which one finds a description of the generally accepted methods of pathological and bacteriological technique, and the book justifies in every detail the position which was accorded the former editions.

Manual of the Diseases of the Eye. For Students and General Practitioners. By Charles H. May, M.D., Chief of Clinic and Instructor in Ophthalmology, College of Physicians and Surgeons, Medical Department, Columbia University, New York, 1890–1903; Ophthalmic Surgeon to the French Hospital, New York; Consulting Ophthalmologist to the Red Cross Hospital, New York; Adjunct Ophthalmic Surgeon to Mt. Sinai Hospital, New York, etc. Third edition, revised, with 275 original illustrations, including 16 plates, with 36 colored figures. New York: William Wood & Co., 1903.

This work contains a clear and terse account of the present state of ophthalmology, so far as this is possible in a book of its size. The reader is never left in doubt as to the writer's meaning. It is easy reading, and we know upon the authority of a famous writer that "easy reading is—hard writing." The author has succeeded in saying enough and not too much, which, as he rightly states in the preface, is the "great difficulty in preparing a book of this sort." Sanity of view characterizes it throughout. One would have to make a somewhat minute search to discover opinions opposed to views now generally held by practical ophthalmologists. We are somewhat surprised at the very little stress laid upon the salts of silver in the treatment of purulent ophthalmia.

This is one of the few books which recognizes that a portion of the accommodation must be kept in reserve during near work, but under the directions for prescribing glasses for presbyopia we do not find that the author is consistent therewith. He subtracts the total accommodation from the amount required for near work and

720

makes good the deficit by glass, allowing no part of the accommodation to be held in reserve.

A high place (but not too high) is given retinoscopy as an objective test of refraction. In competent hands this is unquestionably the most accurate objective method known, rivalling the best results obtainable by the subjective method under the most favorable conditions. In certain cases it is the only reliable method of determining the refraction. The ophthalmometer is accorded its proper subordinate position in the statement that "it is of service when used in connection with other tests." A mydriatic is recommended in all cases of children and young adults in estimating the refraction. Homatropine is declared to be "sufficient for all practical purposes," an opinion with which the reviewer entirely concurs from daily experience.

We note with satisfaction that heterophoria is relegated to a very subordinate place, as in our opinion it deserves. We think that more than enough is granted when neurasthenia, disturbances of digestion and nutrition are set down as possible results of muscular error, even in predisposed individuals; operation is only recommended as a last resort. Disappointment and aggravation of symptoms are truly stated to frequently follow this treatment. The author evidently has little belief in partial tenotomies and advancements.

T. B. S.

Manual of Medicine. By Thomas Kirkpatrick Monro, M.A., M.D., Fellow of and Examiner to the Faculty of Physicians and Surgeons. Glasgow; Physician to Glasgow Royal Infirmary and Professor of Medicine in St. Mungo's College; formerly Examiner in the University of Glasgow and Pathologist to the Victoria Infirmary. Philadelphia and New York: W. B. Saunders & Co. London: Baillière, Tindall & Cox.

Dr. Monro's book should serve admirably the purpose for which it is primarily intended: that of a text-book for students. He has accomplished successfully the difficult task of condensing into a volume of moderate size the enormous mass of facts which makes up our present knowledge of internal medicine. The work throughout shows painstaking care in the classification and arrangement of these facts and in their concise and lucid presentation.

In arrangement it does not differ materially from the usual plan of the larger treatises. The space has been judiciously divided, and each section receives its due consideration. This same sense of proportion is seen also in the space allotted to the individual diseases and to their subdivisions of etiology, morbid anatomy,

symptomatology, diagnosis, and treatment.

The value of the book to students is considerably increased by the prefacing of most of the sections with introductory chapters upon the topographical anatomy, general symptomatology, and methods of examination of the subject in hand.

The section on Diseases of the Nervous System merits especial commendation for its completeness and for the clearness with which

the subject is treated.

Somewhat less full and satisfactory are the chapters upon Diseases of the Stomach. For some reason the subject of Hemorrhage from the Stomach is not considered, although a corresponding chapter appears under Diseases of the Intestines. The somewhat surprising statement is met that epithelioma is one of the four anatomical types of cancer of the stomach!

In addition to the sections usually found in text-books on medicine

there is a short but adequate one on Diseases of the Skin.

L. A. C.

A SURGICAL HAND-BOOK FORTHE USE OF STUDENTS, PRACTITIONERS, HOUSE SURGEONS, AND DRESSERS. By FRANCIS A. CAIRD, M.B., F.R.C.S. Ed.; Assistant Surgeon, Royal Infirmary, Edinburgh; and Charles W. Cathcart, M.B., F.R.C.S. Eng. and Ed., Surgeon Royal Infirmary, Edinburgh. With very numerous illustrations. Twelfth edition. London: Charles Griffin & Co., Limited. Chicago: W. T. Keener & Co., 1903.

As the authors say in their preface, they have endeavored to make this little work of some three hundred pages as practical as possible and as thoroughly in keeping with modern surgical methods as the size of the volume will permit. The mere fact that it is in its twelfth edition is a warrant as to its popularity, at least on the other side of the water. In this edition a number of methods of treatment which are now seldom used have been dropped, and instead have been inserted accounts of the latest technique. It is really worthy of note the amount of useful information the authors have been able to put in such a small book, preserving at the same time the necessary clearness of description.

All minor surgical operations are fully covered and many major ones, while the chapters on dressings afterward and emergency work are most admirable. The illustrations are mostly woodcuts and are diagrammatic, but are clear and show well what is intended. They are very numerous. Special chapters on Surgical Electricity, Massage, Urinc Examination, and Post-mortems seem a little out of place in a work of this character, but are well written and of interest. Written, as it is, as an aid to hospital internes and students, it is excellent and to be highly commended.

G. M. C.

THE MEDICAL EPITOME SERIES. ANATOMY: A MANUAL FOR STUDENTS AND PRACTITIONERS. By HENRY E. HALE, A.M., M.D., Assistant Demonstrator of Anatomy, College of Physicians and Surgeons, Columbia University, in the city of New York. Series edited by V. C. Pedersen, A.M., M.D. Illustrated with 71 engravings. Philadelphia and New York: Lea Brothers & Co., 1903.

THE books of this series are designed by the editor to represent more than the mere quiz compends—to be, in fact, brief manuals of condensed useful information on their respective subjects.

They have, however, for quiz purposes, a list of questions at the end of each general division which serves rather as a guide to the quiz-master than to furnish him actual questions and answers, as is often done, and in which case the continuity of the text is interrupted. This work on Anatomy is clear, concise, and presents more than the mere essentials of human anatomy. It is well written and well printed, while the illustrations are most excellent—far better than those usually seen in short works of this character—and the explanatory notes are clear and well adapted to show the desired point. It is a very good and useful little book.

G. M. C.

A TEXT-BOOK UPON THE PATHOGENIC BACTERIA. FOR STUDENTS OF MEDICINE AND PHYSICIANS. By JOSEPH McFarland, M.D., Fourth edition, rewritten and enlarged. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

During the five years which have passed since the last revision of Dr. McFarland's book much new material has been collected, and the present edition shows the care with which this material has been added and welded into the text. The many references to literature give the book a certain value. The subjects of infection and immunity have been expanded at some length and in places detailed descriptions are given of recent work along these lines of investigation. The chapters upon the pathogenic bacteria are arranged under four main heads: (a) "Phlogistic Diseases," including "Acute Infective Inflammations" and "Chronic Inflammatory Diseases;" (b) "Toxemias;" (c) "Bacteremias" and "Miscellaneous Diseases." Each chapter represents a consideration of the disease or pathological processes caused by that organism, as well as a description of the organism itself. When necessary, closely allied bacteria are also discussed. Since the book deals simply with bacteria, the parasites and protozoa are necessarily omitted. Revisions and additions have been made in various portions of the text, and the present edition will perhaps attract even more attention W. T. L. than the previous ones.

## PROGRESS

OF

# MEDICAL SCIENCE.

#### MEDICINE.

UNDER THE CHARGE OF

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Ochronosis: The Pigmentation of Cartilages, Sclerotics, and Skin in Alkaptonuria.—Osler (Lancet, January 2, 1904, p. 10) reports two cases of ochronosis in patients also suffering from alkaptonuria. This rare condition was first described and named by Virchow in 1866. man, aged sixty-seven years, died of ancurysm, and at autopsy it was found that there was a remarkable blackening of the cartilages of the whole body. The color was coal black, not ochre-colored or yellow. It was more than an ordinary melanosis. Previous to Osler's two cases there have been only seven instances reported in the literature. Two of these cases had melanuria, and in one of them it was definitely stated that the patient did not have alkaptonuria. The seventh case was reported by H. Albrecht in 1902, and to him is due the credit of first suggesting the association of the condition with alkaptonuria. The urinc of his case was dark-colored and reduced copper-sulphate solution, but no homogentisic acid was definitely demonstrated in it. The necropsy in this case showed a general ochronosis. A point of special interest was the gray-blue color of the inner part of the ears, as if due to dilated veins.

Osler's two cases of ochronosis are of especial interest in that the condition was recognized clinically, owing to the pigmentation of the sclerotics and cartilages of the ears, and in one by a remarkable ebonyblack discoloration of the skin of the nose and cheeks. Both of these cases had previously been reported as instances of alkaptonuria, the urine of both showing all the features characteristic of this anomaly. The two patients were brothers. The first is a man, aged fifty-seven years, and the pigmentation now presents the following distribution: The exposed portion of the sclerotics of both eyes show areas of deep-

black pigmentation. The cartilages of both ears, particularly the concha and antihelix, exhibit a remarkable blue-black discoloration. Of particular interest in this ease is the fact that over the nose and cheeks there is a butterfly-shaped area of black pigmentation of the skin. The pigmentation elosely simulates the appearance of powder marks. involvement of the skin has not been previously recorded. The pigmentation had been observed for eight years and it had gradually deepened. The other brother, aged forty-nine years, presented similar pigmentation of the sclerotics and ears, although in a less marked degree. He recently died of some cardiac affection, but no autopsy was obtained. patients had had alkaptonuria for many years, and there was no question but that the pigmentation was that of ochronosis. Alkaptonuria heretofore had been recognized clinically only by the urinary changes. These observations leave little doubt that ochronosis is a part of the malady. At least one of the previously reported cases of ochronosis was proven not to be an alkaptonurie, and A. E. Garrod suggests that there may be two distinct classes of the condition.

Multiple Myeloma (Myelomatosis) with Bence-Jones Proteid in the Urine (Myelopathic Albumosuria of Bradshaw, Kahler's Disease).-F. Parkes Weber (Journal of Pathology and Bacteriology, December, 1903, p. 173) reports a ease of albumosuria in association with multiple myelomata. The patient was a man, aged fifty years, with a definite luetic history. He complained of pain in his loins and of stiffness in the small joints of his hands. Later the upper part of his back began to bend, so that he always stooped. There were no localized outgrowths projecting from the bones, as has been observed in many of the cases reported. The urine contained the so-called Bence-Jones bodies. coagulated at about 58° C., at a temperature much lower than ordinary albumin does; the precipitate almost completely dissolved on raising the urine to the boiling-point, and completely on adding acetic acid, and reappeared on cooling. An interesting feature was the fact that the proteid was occasionally precipitated spontaneously and caused the urine to be turbid when freshly voided. The autopsy showed that there were no localized bone tumors, but that there was a diffuse myelomatous involvement of the marrow of all the bones examined. There was a chronic ulcer of the duodenum, which has led to a severe hemorrhage, causing death.

The presence in the tumor eells of certain granules and globules of various sizes constituted a striking histological feature in the case. Prof. R. Muir, of Glasgow, who examined the growth, expressed his opinion as follows: "That the tumor is formed by a special and characteristic type of cell, which is probably derived either from the neutrophilic myelocyte or its predecessor; that the cell produces in its protoplasm, in a granular form, a substance which is closely allied to, though not quite identical with, the substance of the neutrophile granules; and that this substance is formed in excess and may form larger granules by confluence of the smaller, the larger globules sometimes becoming free."

The nature of the Bence-Jones bodies is considered at some length. The view advanced by Magnus-Levy, that it is a non-assimilated digestive proteid, is opposed, because in this case alteration of the diet had no effect on the excretion of the albumose, and as much was eliminated during the night as during the day. The view that this proteid is pro-

duced in the bone-marrow is supported, and the suggestion is thrown out that the curious granules found in the specific cells of the tumor

may possibly be its source.

Weber has collected the cases of Bence-Jones' albumosuria from the literature, and finds that, including his own, there have been thirty-five undoubted instances recorded. In addition to these there were four doubtful cases.

Family Diabetes.—MARTINET (La presse médicale, February 10, 1904, p. 94) reports that in June, 1900, a man, aged forty-eight years, consulted him for symptoms which proved to be those of diabetes mel-The disease had followed an attack of influenza contracted in the previous February. The patient's father had died of diabetes also.

Several months later the writer was consulted by the patient's wife, a woman aged forty years. She was found to have exophthalmic goitre. The examination of the urine showed a large amount of sugar present. Martinet considers this a typical ease of conjugal diabetes, although some objection might be taken to this opinion, owing to the not infrequent occurrence of glycosuria in exophthalmic goitre. He states that he observed four eases of eonjugal diabetes in his practice during the year 1903, and does not believe that the condition is extremely rare.

At the beginning of this year the mother of the first patient, aged sixty-six years, came under treatment for a phlegmon on the right hand, which developed very rapidly after being pricked with a needle. The examination of this patient's urine also showed abundance of sugar.

She lived with her son.

In this family the patient, his mother, and his wife had diabetes and his father died of the disease. The writer lays down the following axiom: If one discovers diabetes in one or several members of a family, the urine of all the other members should be examined for sugar, especially if the various members live together.

The Reactions of the Blood in Diabetes Mellitus: A Contribution to Our Knowledge of the Thermolabile Complements.—Sweet (Journal of Medical Research, October, 1903, p. 255) carried out a series of experiments with the view of ascertaining, if possible, the cause of the abnormal susceptibility of diabetes to infectious processes. The experiments were made on the blood of dogs rendered diabetic by the extirpation of the pancreas. The washed red cells of guinea-pigs and rabbits were used for testing the hæmolytic activity of diabetic dogs' serum. His experiments seem to afford the first adequate explanation for the frequency of infections in diabetes mellitus.

The writer's more important results may be summarized as follows: The complete removal of the pancreas from dogs, which causes a true diabetes inellitus of a severe type, is followed by a marked decrease of the hæmolytic activity of the diabetic dog's scrum for both rabbit's and guinca-pig's crythrocytes. The diabetes caused by the complete extirpation of the pancreas is further characterized by what is to be interpreted as a complete loss of the normal bactericidal property of the serum of the dog. This he demonstrated conclusively for B. coli communis, B. typhi abdominalis, and for B. dysenteria. The demonstration of the decrease of bactericidal power of the diabetic serum for staphylococcus pyogenes aureus was not so conclusive, for the reason that the normal

serum of the dog has very little if any bactericidal effect upon this organism. The decrease of the hæmolytic activity of the serum of the diabetic dog is due to loss of hæmolytic complements. The loss of bactericidal power is, from analogy with the hæmolytic phenomenon, doubtless to be interpreted as due to a loss of bacteriolytic complements. The complete removal of the pancreas is as necessary to this loss of complements as it is to the production of a diabetes. The complete removal of the pancreas does not deprive the organism of its power to react to the inflammatory process by an increase of the complementary substances. The loss of the complementary substances in diabetes melli us points conclusively to the fact that no relation exists between the leukocytes of any type and the production of the complements.

#### SURGERY.

#### UNDER THE CHARGE OF

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On the Use of Rubber and Thread Gloves.—Godfel (Centralblatt für Chirurgie, 1903, No. 42) states that in view of the fact that rubber gloves tear very easily and that thread gloves are very permeable, it is a good procedure to wear the latter over the former, which not only prevents the slipping of instruments, etc., but also has the following advantages: 1. It is a greater safeguard against infection, either of the patient by the operator or vice versa. 2. The hands can be used more freely and easily. 3. The gloves can be rapidly changed should necessity require. 4. The use of the thread glove does quite away with the slipperyness of the rubber, and so ligatures may be tied more easily and securely. 5. The thread gloves can be easily removed in any case where their roughness might injure the tissue and then be replaced when the danger is passed. 6. The time of the operation is shortened. 7. By their use repeated washing of the hands becomes unnecessary, as the gloves can be scrubbed while on the operator's hand, and this prevents chapping or eczema in those cases where the hands are very sensitive.

Three Cases of Rupture of the Intestines without External Lesion.
—Senereano (Bull. et mém. de la Soc. de chir. de Bueharest, 1903, Nos. 3 and 4) states that during the past year he has had three such cases present themselves for treatment, respectively, twelve hours, twenty-four hours, and thirty-eight hours after the receipt of the injury. The first patient had an old and reducible right-sided hernia, and gave a history of having received a sharp blow in the right iliac fossa. He

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entered the hospital on the next day, and in the afternoon was given a purgative. The next day he was in a very grave condition, presenting the symptoms of an intestinal lesion, but nothing characteristic. An exploratory incision was made as for hernia or appendicitis; the hernial sac was found empty and there was no strangulated intestine. The incision was then enlarged, the excum and appendix were found to be normal, but the entire abdominal cavity was filled with intestinal contents, and 25 cm. from the excum was a perforation which admitted the little finger. This was closed, thorough lavage of the abdominal cavity was then performed and the wound closed; the patient made a good recovery. The second case had an old and reducible hernia upon the left side. He was kicked in the abdomen to a horse and twenty-four hours later was admitted to the hospital. Upon operation on the third day, it was found that there was a perforation of the small intestine, and that the abdominal cavity was filled with intestinal contents. The perforation was closed, the abdominal cavity irrigated, and then the wound closed. The patient recovered. The third patient had no hernia, but had received a blow upon the abdomen, which was opened in the median line. Two perforations were found near the excum about 8 cm. apart. They were closed and the abdomen washed out. This patient also made a good recovery.

Actinomycosis of the Liver.—Auvray (Revue de chir., 1903, No. 7), after an admirable and exhaustive review of the subject, states that medical treatment by the iodide of potassium has proven to be of no value in these cases. Although the number of cases is small, still, it may be well said that this treatment has been followed by good results when the disease is localized elsewhere, and in every case it would seem to be a valuable adjunct of the surgical treatment. The author reports the surgical treatment of six cases in which the liver was involved, but it is to be regretted that some of these reports are quite incomplete as regards the exact operative procedure in the individual case. These cases all presented some form of abscess, and there are three ways of reaching and evacuating such a purulent collection: 1. By way of the abdomen, the usual method. 2. The thoracie route. 3. The lumbar route. In four of the cases the abscess was opened through the abdomen, in some the operation merely consisted in a simple incision of the abdominal wall, while in others a formal laparotomy was necessary, with a resection of the ribs in an effort to discover the exact point of the infec-The only complication during these operations was in one case in which there was an abundant hemorrhage. The lumbar route was used in only one case; the incision was made parallel to the last rib, and then the abseess was punctured with a trocar and evacuated. thoracie route was followed in one case without a previous resection of the ribs. These six cases were all eventually fatal, but not as the result of the operative interference; the results might have been better had the operations been performed earlier-in other words, before the formation of an abseess.

Suture of the Patella: A Practical Study Based upon Seventy Operations.—Lucas-Championniere (Archives internationales de chirurgie, 1903, No. 1) states that the first antiseptie operation of suturing of the patella was performed by Cameron, of Glasgow, in

1877. At this time Lister also reported his first ease, and in 1883 he was able to note six more, and clearly showed that this new method of treatment was followed by a perfect recovery, whereas in the past the condition had been looked upon as being of necessity followed by lameness. In view of the fact that fracture of the patella is comparatively rare, the author's experience of seventy eases is quite remark-A study of these cases shows that the only rational method of treatment is a free incision of the joint; the evacuation of its morbid eontents, such as blood; the accurate apposition of the fragments by suture, and then the repair of the torn synovial membrane, and this is the only way in which good union can be secured. The best suture material is silver wire, which is in itself antiseptie. Care should be taken to have absolute asepsis, and the joint should be thoroughly flushed out with a 5 per cent. solution of earbolic acid. The best time to operate is either two, three, or four days after the aecident, and not within the first twenty-four hours. The wound should be drained for four days, and there should be passive motion at each dressing. The patient should be allowed to walk in from ten to fifteen days. clusion, the author reports in detail many of the more interesting and complicated eases of the series.

#### THERAPEUTICS.

UNDER THE CHARGE OF

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Light Therapy.—Dr. Kellermann considers that the use of dark-blue incandescent light produces excellent results when locally applied in neuralgia and eczema, and his statistics seem to prove his assertion. He also states that the treatment may be applied in leg uleers. The duration of each treatment is not more than fifteen minutes and the number of sittings should not be more than four per week. He believes that the beneficent effect is due chiefly to the action of dry heat, and that the chemical or specific action of the light rays plays a very subordinate part in producing the result. His article contains a report of numerous eases which have undergone the treatment.—Zentralblatt für die gesamte Thérapie, 1904, No. 1. p. 16.

Serum Therapy in Plague.—Dr. Victor Godinho, in his plague service at the hospital in San Paulo, Brazil, has employed a serum made after the manner of the plague serum prepared at the Pasteur Institute, and reports upon its use as follows: The minimum dose injected was 150 e.é. to 200 e.c. When injected during the evolution of the disease no abortion of the malady took place and the buboes appeared as usual, but their pain was lessened and sudorific erises and defervescence by lysis were produced. Intravenous injections of 20 e.e. to 40 e.c. of the

serum would cause a rise in temperature of a degree, followed by abundant perspiration and a fall of two or three degrees. In some patients it seemed as if the crisis of the disease was brought about by the serum, since the temperature fell and did not rise again after its use. Certain transitory symptoms, such as chill, agitation, dyspnœa, cyanosis, vomiting, etc., were caused by the injections. When administered before the third day of the disease the serum almost always brought about a cure in adults, but did not influence the development or the suppuration of the buboes. The course of the disease being much more violent in children makes it imperative that the serum should be used as early as possible. The occurrence and course of pneumonia as a complication did not seem to be influenced by the serum. Those suffering from the septicæmic form of the disease bore the serum well, but its good effects were less marked than in those affected with the bubonic type. Lastly, the serum did not prevent the termination of the disease by cachexia. In conclusion, the author states that the use of the serum, like that of diphtheria antitoxin, results favorably in certain cases, but not in all.—La presse médicale, 1904, No. 8, p. 60.

Suprarenal Opotherapy.—Dr. A. Gov states that in connection with this subject the following conclusions have been reached: 1. That the administration of the suprarenal extract slows the pulse by stimulating the pneumogastric. 2. That it strengthens the cardiac systole by direct stimulation of the heart muscle and by stimulation of the cardiac ganglia. 3. That it causes an increase in blood pressure due to contraction of the capillaries through stimulation of their vasomotor nerves and muscle fibres and by action upon the vasomotor centr. 4. That it blanches and causes an anæmia of the tissues. The primary therapeutic application of the extract is in Addison's disease and in the treatment of certain symptoms of suprarenal insufficiency. In Addison's disease in a short time the extract causes a diminution in the pigmentation and a rapid increase in body weight. In experimental physiology the extract has been employed as an intravenous injection as an heroic remedy in animals in chloroform syncope. An important consideration is that the preparation used should be of definite strength.—Revue francaise de médecine et de chirurgie, 1904, No. 3, p. 64.

The Treatment of Hepatic Colic.—The indications to be met in this condition are these: to relieve the pain; to bring about a favorable issue of the crisis by facilitating the passage of the calculus; to prevent complications. The pain may be relieved by the hypodermic use of morphine in connection with atropine. This latter should be most carefully given when there is tendency to collapse. To patients who bear morphine badly chloroform to the obstetrical degree may be given, or if there is no vomiting the following formula: Chloral hydrate, 2; syrup of peppermint, 30; chloroform-water, 100. Dose, two dessertspoonfuls every quarter-hour until relieved. When the stomach is intolerant the chloral may be given per rectum, thus: Chloral hydrate, 2 to 3 parts dissolved in 10 parts boiling water mixed with the yolk of an egg, to which mixture 1 part of wine of opium and 200 parts of milk are added. Ether and turpentine, on the one hand, and olive oil and glycerin, on the other, are the remedies most usually employed to facil-

itate the passage of the stone. The latter agents are preferable. The great difficulty is to overcome the repugnance of the patient to the olive oil. Toward this end the oil may be stirred up with a little beer, or to it may be added a little menthol or a few drops of essence of bitter almonds or anise. The quantity of the oil should be from four to eight ounces. Glycerin is more acceptable to the patient, but less effective. Finally, the spasm of the bile-ducts may be relieved by the application of hot-water bags to the abdomen. Of the complications of hepatic colic, the most formidable is heart-failure. To combat this it is wise to substitute for the atropine, so frequently given with the morphine, a heart stimulant, such as sparteine. Chloral should not be given where collapse is threatened, and in this juncture hypodermic injections of camphor in olive oil are useful. To prevent accidents to the biliary passages, we should avoid the use of purgatives and suspend food until the pain has ceased for several hours. Rupture of the bilepassages necessitates immediate surgical interference. Revue francaise de médecine et de chirurgie, 1904, No. 5, p. 115.

Iodized Oil in Simple Goitre.—DR. DUBAR reports two cases of simple goitre in young girls which he has treated by injections of oil containing 40 per cent. of iodine. He injected very slowly at intervals of about one week fifteen drops of the oil into the substance of the gland. Each injection was made into a different part of the gland, and while in no case was there any unpleasant reaction, two or three of the injections were followed by the appearance of a small, firm node showing no signs of inflammation. These eventually disappeared. In one patient, after a series of nine injections, the size of the goitre was diminished by three-fourths of an inch. In the other six injections resulted in a diminution of nearly one inch, and a series of four more injections caused a total shrinkage of nearly an inch and one-half.—Le progrès médicale, 1904, No. 4, p. 50.

Sodium Bicarbonate in Gastropathies and Other Diseases.-M. HENRI HUCHARD, in a paper upon dyspepsia, deals at length with this therapeutic agent. In anorexia he believes it to be indicated in small doses (3 to 5 grains), since, taken a half-hour before eating, it increases gastric secretion and excites the contractility of the stomach. In this connection he considers it far preferable to the bitters. In hyperchlorhydria, since here we have an excess of gastric secretion, the drug should be prescribed in large dosage at the end of the period of digestion, at about the time when the gastralgia is likely to appear-that is to say, about two or three hours after the meal. In this condition the author gives 4 or 5 drachms daily of the salt for several weeks at a time, and finds no resulting evil effects; on the contrary, oxidation and metabolism are favored, and an increase in body weight often takes place. The gastric crises of tabes, when these are accompanied by hypochlorhydria, respond well to sodium bicarbonate given in doses of 5 drachms per Also the drug produces excellent results in the migrainiform affection termed nervous gastrotoxia. Undoubtedly, when the drug is given improperly, various bad effects may follow; even anæmia may be produced, but these results are not to be considered the fault of the alkali, but of the prescriber. Sodium bicarbonate is the remedy par excellence in diabetes, in the prevention of coma, which condition is

characterized by a true acidemia. The dosage in this disease should be at least 2.5 drachms daily, and where coma actually exists as large a quantity as 3 ounces may be given. In dermatoses, especially those of arthritic origin, alkaline medication has a distinct sphere, and in such conditions the bicarbonate is indicated in doses of 3 or 4 drachms per day. In biliary lithiasis and hepatic colic there is, in the author's experience, no surer method of cure than regular alkaline medication employed in massive doses.—Revue de thérapeutique, 1903, No. 2, p. 37.

The Treatment of Thrush.—DR. MERLETTI has found that the treatment of this affection by successive applications of hydrogen dioxide and sodium borate solutions is to be recommended. These two agents produce an abundant froth, which acts rapidly upon the ordium albicans. The author has employed this procedure in a great number of cases, and is convinced that, when repeated three times every twenty-four hours, it will bring about a cure even in marked cases of the confluent type of the disease. If the treatment is instituted at the beginning of the affection two or three applications are sufficient to stop the growth of the fungus.—Journal de médecine de Paris, 1904, No. 4, p. 31.

#### OBSTETRICS.

#### UNDER THE CHARGE OF

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The Induction of Labor for Contracted Pelves.—In the Archiv für Gynákologie, Band lxx., Heft 3, 1903, Hahl gives the result of 84 cases in the Obstetric elinic of Helsingfors in which labor was induced for contracted pelvis. His statistics cover the practice of the Clinic for thirty-two years and the eases occurred among 23,000 patients. The relative frequency of the operation was one in 274 confinements, or 0.365 per cent. In Leopold's clinic the operation was done once in 131 patients, and in a subsequent series of cases once in 151 patients. Braun's statistics give one in 441 patients; Chrobak one in 627; Pinard one in 150, and Walter one in 165.

The smallest true conjugate in these cases were 7 cm. in three and 7.5 cm. in one case, a flattened and symmetrically contracted pelvis. The earliest period of gestation at which pregnancy was interrupted was thirty weeks in one case, and the latest thirty-eight weeks in seven eases. The average was from the thirty-fifth to the thirty-sixth week.

In seven eases the fœtus was in a transverse position. This was corrected by version or spontaneous evolution. The complications which occurred during the labors were transverse presentation in 5 cases, breech presentation in 2, prolapse of the cord in 3, lateral placenta

prævia in 1, and threatened rupture of the uterus in 1; 29.76 per cent. of the cases terminated in spontaneous birth; 70.24 per cent. required Version was done most frequently and then forceps.

Craniotomy was performed but twice, or 3.38 per cent.

The results of this series of cases were as follows: The maternal mortality was 2.38 per cent. from all causes. From septic infection alone the mortality was 1.19 per cent. The maternal morbidity was 7.23 per cent. Of the 84 children, 75 per cent. were born living and 25 per cent. were stillborn; 59.52 per cent. were discharged living from the hospital, while 13 of the 63 children born living died in the hospital during the first two weeks. Of the children who left the hospital living, 84 per cent. survived for a year, which was one-half the entire number of children born alive.

Mechanical Dilatation of the Cervix during Pregnancy and Labor. -De Seigneux (Archiv für Gynäkologie, 1903, Band lxx., Heft 3) criticizes Bossi's dilator because it has no pelvic curve, cannot be taken . apart for cleansing, and cannot readily be shifted to vary the line of application of its force during its use. To correct these faults, he has invented an instrument resembling Bossi's in its general principles, having a pelvic curve and which can be taken apart for cleansing and whose branches are so placed upon the joints that they exercise force in various directions. He reports seven cases in which his instrument was used by himself and others with satisfaction.

Prolapse of the Placenta from its Normal Situation.—In the Archiv für Gynäkologie, 1903, Band lxx., Heft 3, Kayser reviews extensively the literature of this subject. He finds in the records of the Clinic at Dresden no case of prolapse of the placenta recorded in 22,000 births. In the Clinic at the Charité there was recorded no case in 42,800 births. On examining the records, a case of version with bleeding is described which must have been a prolapse of the placenta. A few cases collected from the literature are quoted in which this accident happened.

His own case was that of a multipara, aged thirty-three years, who had a considerably contracted flattened pelvis. Eight hours after the rupture of the membranes, the head presenting, fetal heart sounds became much less frequent. On examination, the placenta was found presenting at the internal os, although formerly it could not be discov-There was slight hemorrhage. Prolapse of the placenta was diagnosticated and version was performed, which was accompanied by a slight discharge of blood. The fœtus was not extracted, but was allowed to remain in the uterus in the hope that labor pains would come on. Fifteen hours after the performance of version the patient was found in collapse and shock. The cervix was incised. The body of the child was delivered with difficulty and the head was delivered by craniotomy. The patient died during the operation. Upon autopsy the attachment of the placenta had been at the fundus of the uterus. A transverse rupture of the uterus was found on the anterior wall of the cervix, while upon the right side was discovered a dermoid cyst. It was Kayser's belief that the rupture of the uterus occurred while an assistant made strong pressure upon the after-coming head in an effort to press it downward into the pelvis.

From the cases reported and from this own, Kayser deduces the

following conclusions: In the presence of prolapse of the placenta with hemorrhage, delivery is imperative. A high degree of pelvie contraction forbids the performance of version. Embryotomy is usually indicated.

If hemorrhage be absent and the child be living, an effort should be made to save its life. Delivery should then be conducted in the manner least dangerous for mother and child. If the child is dead and the pelvic measurements are normal, immediate interference is unnecessary.

A Contribution to the Etiology, Symptomatology, and Treatment of Ectopic Gestation.—Runge (Archiv für Gynäkologie, 1903, Band lxx., Heft 3) reports 233 cases of ectopic gestation from the Charité and Polyclinie in Berlin. There were 125 cases of recognized pregnancy and 108 eases of hæmatocele. Among the cases of pregnancy, 73 were tubal abortions, 47 ruptures of the tube, and 5 intact tubal pregnancy. Among the unusual cases were one treated by posterior colpotomy in which the tube was removed with the ovary; one ease of interstitial pregnancy; one case of ectopic gestation in which a living child was delivered by abdominal section, the child surviving and the mother afterward dying from purulent peritonitis, and one case of tubal abortion with suppuration.

So far as the results were concerned, from the 73 cases of abortion, 36 recovered without operation and 36 recovered after operation. One case died after operation. In 47 cases of rupture of the tube, five were treated without operation and recovered. Forty-two were operated upon, of whom 31 recovered and 11 died. This gives a mortality of 1.4 per cent. in tubal abortion, and 23.4 per cent. in ruptures of the tube. Eight of the deaths resulted through anæmia from hemorrhage and 3 from septic infection. In one case the cause of death could not be distinctly made out. The entire mortality for cases of rupture,

excluding those dying upon the operating table, was 6.4 per cent. In 108 cases of hæmatocele, 37 were treated by operation; 25 of these were done by incision through the posterior wall of the vagina. Seventy-one eases were treated without operation, and of these one died. This patient perished from purulent septic peritonitis. patient died after operation from infection of the hæmatoccle.

Runge's conclusions in the study of his cases are as follows: He believes that the principal eauses for tubal gestation are infection during the puerperal period and gonorrhea. It is, however, true that women who have not been previously pregnant are not exempt from ectopic gestation. A period of sterility in most cases precedes the period of cetopie gestation. Tubal abortion and rupture occur most frequently from the first to the third month of pregnancy. In these cases operation is to be undertaken when conditions threatening life arise, when the tumor increases rapidly in size, when the general eondition of the patient grows worse and resorption of the tumor does not occur, and when the patient has long-continued fever. Abdominal section without drainage is best for these eases and the placenta and fetal sae should be removed entire if possible. Only those blood elots which can be readily reached should be removed unless the blood is decomposed and In view of the risks of abdominal pregnancy, it is not well to wait until the child is viable.

Hæmatoecle should, if possible, be treated without operation.

method of election is by incision of the posterior vaginal wall, abdominal section being reserved for those cases in which the tumor is large and in which it cannot safely be reached through the vagina.

The Morbidity of the Puerperal State in Cases Complicated by the Birth of a Macerated Fœtus.—Kothen (Archiv für Gynäkologie, 1903, Band lxx., Heft 3) reviews the literature of the subject, in which he has collected 358 cases of labor complicated by death and maceration of the fœtus. In 34 of these cases some complication arosc during the puerperal period. A morbidity of about 10 per cent. was observed. The second series of 274 cases was observed, 157 of which made normal recoveries, although the fœtus had been considerably decomposed. Spiegelberg ascribed morbidity in these cases not to the death of the fœtus, but to outside contamination in the conduct of labor. Klein injected into animals an extract of the tissues and organs of a fœtus which perished about fourteen days before its birth. Two animals died after such injection. The symptoms of death were those of toxemia, as the injected material was proved by culture to be sterile of bacteria.

Kothen's cases were 70 in the Clinic at Giessen. Fever was considered present when the patient's temperature rose above 99.5° F. at any time. In 14 of these cases, or 20 per cent., the temperature rose. In 27.1 per cent. some abnormality followed the birth of a macerated fectus. In comparison with the general morbidity of other puerperal patients, the death and maceration of the fectus increases the complications of the puerperal period by 10 or 11 per cent. In none of these cases was the death of the mother traceable to a macerated and dead condition of the fectus.

Kothen concludes from a study of this subject that an increased morbidity of from 10 to 11 per cent. over the ordinary morbidity of labor and the puerperal state is observed in cases where the fœtus is macerated. A foul condition of the lochia is apt to be present in these cases.

#### GYNECOLOGY.

UNDER THE CHARGE OF HENRY C. COE, M.D., OF NEW YORK.

ASSISTED BY

WILLIAM E. STUDDIFORD, M.D.

New Method of Ventrosuspension.—Bardescu (Zentralblatt für Gynäkologie, 1904, No. 3) describes the following method of suspension of the uterus: The uterus is drawn upward with a volsellum after the separation of adhesions. An incision is made through the fascia and rectus muscle on either side of the wound, and each round ligament is seized in turn with a bullet-forceps and the loop is drawn through

the opening and secured with four catgut sutures. The fascial edges are then united, after which the loops are sutured together in the median line. The patient is kept on her back for ten or twelve days, the urine being drawn by catheter until the third day.

Care should be taken not to elevate the fundus uteri above the

symphysis, or to approximate it too closely to the abdominal wall, in

order to preserve the normal relations and mobility of the organ.

Causes of Sterility.—In a discussion of this subject before the Dutch Gynccological Society (Zentralblatt für Gynäkologie, 1904, No. 3) KOUWER stated that in 700 private cases sterility was noted in 101, 11 being due to impotence in the husband. The speaker had been successful in treating less than one-half of the cases in which this was the main symptom for which relief was sought (24).

Treub had noted 39 eases out of 188 in which the husband was at fault. In 80 cases occurring in married women where the semen was examined, he found azoöspermia in 25 and oligozoöspermia in 12. The speaker said that he always examined the husband's semen if

possible.

Lysol Poisoning.—Hammer (Münchener med. Wochenschrift, 1903, No. 21) reports several cases in which intrauterinc injections of lysol solution were followed by unpleasant results. From experiments on animals, he concluded that the use of strong solutions was not advisable. In a purperal case fatal thrombosis occurred from the entrance of lysol into a vein (the strength of the solution was not stated).

Torsion of the Uterus.—Petit (Semaine gynécol., June 30, 1903) reports a case of laparotomy for severe dysmenorrhea and menorrhagia in which adhesions confined to the left side of the pelvis had caused a half-turn of the uterus around its long axis from right to left, so that the right adnexa were situated behind the left broad ligament below a cystoma of the left ovary.

A New Method of Preventing Ventral Hernia.—NIKONOW (Jour. akus. i Shenbolesnej; Zentralblatt für Gynäkologie, 1904, No. 3) reports a series of cases in which the following procedure was adopted: In opening the abdomen an incision was made about two inches to one side of the median line. After opening the anterior layer of the sheath of the rectus, the muscle is separated by blunt dissection and is drawn outward so that the posterior layer and peritoneum can be incised in the median line.

At the close of the operation the peritoncum and posterior fascial edges are closed separately, then the muscle's replaced and the anterior layers of the fascia and skin are sutured. The writer believes that this is a sure way of preventing subsequent hernia.

Results of Vaginal Hysterectomy for Cancer of the Uterus.—FLAISCHLEN (Zentralblatt für Gynäkologie, 1903, No. 52) reports a series of 48 cases in which the cancerous uterus was removed per vaginam. Four patients died from the operation; recurrence occurred in 24. Seventeen were living after an interval of eight years; 12 were free from recurrence after ten years; 9 were well after thirteen years. The writer

contrasts these results with Pozzi's pessimistic statement that out of 204 cases he could report only 2 permanent cures, and believes that his favorable statisties are explained by the fact that in every instance an early diagnosis was made. This supports Winter's statement that the success of the surgical treatment of uterine cancer in the future will depend more on the early recognition of the disease than on the radical nature of the operation, and, in the writer's opinion, proves that radical abdominal hysterectomy will not supplant the vaginal method.

Comparison of Vaginal and Abdominal Hysterectomy for Caneer.—Olshausen (Zeitschrift für Geb. u. Gyn., Band l., Heft 1) reports 206 vaginal hysterectomies for cancer with 15 deaths, and 4 abdominal with 1 death during the years 1901 and 1902. He prefers the vaginal route until statistics extending over five years shall prove that the results of the abdominal method are better. The fact that Wertheim hopes that from 15 per cent. to 18 per cent. of his cases will be permanently cured by the radical operation does not convince the writer, as his own cures have been 18 per cent.

Conservative Surgery of the Adnexa.—TREUB (Annal. dc gyn. ct d'obstétrique, 1903, No. 5) deprecates hasty resort to a radical operation in cases of adnexal disease, since these rarely result fatally. In 612 cases of salpingo-oöphoritis a more or less complete cure was obtained in 80 per cent. by non-surgical treatment—rest, ice-bags, hot douches and tampons. The mortality after radical operations is from 5 to 6 per cent., and patients are not always relieved of pain, aside from the fact of subsequent climacteric disturbances.

The writer performs posterior section when possible, and when the abdomen is opened always tries to preserve portions of tubes and ovaries, except in cases of tuberculosis, when he extirpates the uterus

with the adnexa.

Premature Menopause.—Siredex (Comptes-rend. de la Soc. d'obstétrique de gyn. et de paed., December, 1903) reports 5 cases in women whose ages ranged from twenty-two to thirty-five years. Three were in good health; in one menstruation ceased after typhoid fever, though no direct causal relation could be established. One patient subsequently developed diabetes, from which she died. In all menstruation had previously been somewhat scanty, and three had been sterile. Climacteric disturbances were slight. The usual anatomical changes, especially atrophy of the cervix, were well marked. Treatment in true cases of premature menopause is useless.

The Adnexa in Cases of Uterine Fibroids.—Daniel (Revue de gyn. et de chir. abdom., 1903, No. 1) found pathological changes in 59 per cent. of the cases which he observed. Catarrhal salpingitis was present in one-fourth of the operations, pyosalpinx and pachysalpingitis in others. Hydrosalpinx and hæmatosalpinx, tuberculosis of the tubes, and ectopic gestation were all noted.

The ovaries were more frequently diseased than the tubes (40 per cent.), cystic degeneration, cystoma, and abscess being most common. The writer attributes the adnexal changes to three causes, viz.: 1. Infection.

2. The "fibromatous diathesis," marked by vascular changes

which lead to hyperplasia of fibromuscular tissue. 3. The presence of the uterine fibroids, which causes obstruction in the tubes, with resulting

lıydrosalpinx or hæmatosalpinx.

Notwithstanding the relative frequency of tubal and ovarian disease accompanying fibroids, this is frequently unrecognized before operation. It should be suspected if the patient complains of pains in the ovarian regions, since these are caused by fibroids only when the latter arc impacted. Sterility in women with fibroids is usually due, the writer believes, to disease of the adnexa.

Complicating Uterine Fibroids.—STRASSMANN (Zen-Pyosalpinx tralblatt für Gynäkologie, 1904, No. 4) reports 3 eascs (2 of his own and 1 of Lomer) in which pyosalpinx accompanied calcified fibromyomata. He believes that there is a direct causal relation between the two con-While the tubes may be infected as the result of septic or gonorrheal endometritis occurring in a fibroid uterus, pus is rarely found at operations. He infers that prolonged pressure of hard uterine tumors is apt to cause occlusion of the tubes, with the subsequent formation of pus (if baeteria are present) just as occurs in the case of renal calculi.

The Adnexa in Cases of Fibroid.—Daniel (Revue de Gynécologie, Band vii., Heft 2-4) finds that in 207 eases only one-third of the cases of diseased adnexa in connection with fibroid uteri were due to infection. In over one-half there was a diffuse genital "fibromatosis," due to vasomotor or reflex influences. In some eases pressure may be the eause of adnexal disease, as in unilateral hydrosalpinx. The diagnosis is aided by the presence of ovarian disturbances, pressure in the bladder and rectum and symptoms of torsion; 3.68 per cent. of the fatal cases are due to adnexal complications.

Fibroids and Sterility.—Austerlitz (Prager med. Wochenschrift, Nos. 23 and 24, 1903) among 339 eases of uterine fibroid found primary sterility in 20.23 per cent. and secondary in 21.25 per cent., as compared with 4.17 per cent. and 13.68 per cent. in women without such neoplasms. The writer was unable to demonstrate whether sterility was directly duc to fibroids or not; 51.2 per cent. of women with interstitial tumors were primarily sterile; 22.2 per cent. of the mixed variety; 16.9 per cent. subscrous, and 12.7 per cent. submucous.

Appendicitis and Dysmenorrhea.—Mérigot de Treigny (Revue prat. d'obstétrique et de gyn., 1903, No. 12), in reporting a case illustrating the difficulty of diagnosis between these conditions, quotes from Legendre to the effect that intestinal troubles are apt to be aggravated during menstruation, pain being localized, especially over the appendix. The muscular rigidity characteristic of appendical inflammation may be present. The pains sometime cease at once after the discharge of mucus from the bowel. The symptoms simulate those of recurrent rather than acute appendicitis, and the pain is apt to shift from McBurney's point, while the patient's general condition is not such as to suggest the presence of peritonitis.

In the case reported by the writer a girl, aged eighteen years, had

severe abdominal pain during menstruation, with obstinate constipa-

tion. The pains were sometimes localized over the appendiceal region, although they were again equally severe over the left lower abdomen. They were generally relieved by laxatives. As they became intermenstrual and were evidently of intestinal origin, an incision was made over the appendix, which was found to be thickened and adherent. After its removal the pains disappeared; the patient married and had a normal confinement. The writer raises the question whether so-called intermenstrual pain may not often be of appendiceal origin.

#### OPHTHALMOLOGY.

UNDER THE CHARGE OF

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AND

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Resection of the Cervical Sympathetic Ganglia in Glaucoma.—WILDER, Chicago (Annals of Ophthalmology, January, 1904), gives a summary of 68 operations, 7 by himself. Of these operations, 38 were for simple glaucoma, 16 for chronic inflammatory glaucoma, 4 for subacute glaucoma, 3 for acute glaucoma, 4 for absolute glaucoma, 2 for hemorrhagic glaucoma, 1 for buphthalmos; 5 operations were preventive, in none of which has glaucoma occurred. One death occurred. Of the 38 operations for simple glaucoma, 14 gave no improvement whatever, 5 were temporarily improved for periods from fifteen days to eight months, but had recurrent attacks that necessitated iridectomy or eaused loss of the eye; 15 were improved as long as they were under observation for periods of from two months to two years. Of these, 3 were stationary, 1 died, 6 remained unimproved after iridectomy, but improved after sympathectomy.

Of the 16 operations for ehronic inflammatory glaucoma, 4 were improved, 3 temporarily, 3 remained stationary, and 6 were unimproved. Of the 4 operations for subaeute glaucoma, 3 were improved and one temporarily. Of the 3 operations for acute glaucoma, 1 improved, 1 improved temporarily, and 1 remained stationary. Of the 4 cases of absolute glaucoma, 1 was improved, 3 unimproved. Both of the cases of hemorrhagic glaucoma were improved. The case of

buphthalmos was improved.

The results in this series of eases do not seem as favorable as those presented by some others; thus Rohner reports 79 improved of 114 operated on. However, there seems a field for this operation, for cases have been reported in which selerotomy and irideetomy had failed and in which sympatheetomy reduced tension and improved vision.

The simple ehronic form seems the most suited next to the hemorrhagic. If the operation is to be performed at all Abadie's rule holds:

In acute and subacute glaucoma, iridectomy first; if that fails, sympathectomy; in simple glaucoma myotics twice a day; if in spite of them the vision fails, sympathectomy.

Toxic Amblyopia Caused by Wood (Methyl) Alcohol.—Buller, Montreal (Montreal Medical Journal, January, 1904) reports 3 cases of this lately described affection. The amount taken was about a wincelassful; in the third case three such doses were taken. In cases 1 and 2 the vision was reduced to counting fingers from three to eight fect. In Case 3 the vision was about a quarter of normal and improving. In each of the cases there was, as usual, improvements with quick relapses. In all 3 cases there was evidence of optic atrophy; the third showed only slight pallor of the papillæ.

The pathogenesis of wood aleohol blindness is still a matter of dispute, some holding that the primary lesion is in the retrobulbar portion of the optic nerve and others that it is in the macular region of the retina. Buller considers the optic nerve to be primarily at fault.

Wood alcohol is used in many trades and manufactures, and as even working with materials largely containing it, such as varnish, can induce poisoning from the vapor alone, the public should be informed of the dangers to sight from this substance.

Delirium after Eye Operations.—Finlay, Havana (Archives of Ophthalmology, January, 1904) reports a case of violent delirium following extraction of cataract in a woman sixty-six years of age. Operation of the second eye was followed by nervousness but none of the excitement of the first. Atropine not having been used, could be excluded as the cause, and so could darkness, the patient being in a ward where there was a superabundance of light and air. Alcoholism was not a factor. The twenty-four hours' urine was found to be remarkably scanty and the proportion of urea considerably diminished. Traces of sugar and albumin were also present.

Finlay considers this case as confirmatory of Fromaget's view that such delirium is the result of an autointoxication most often uramic, in accordance with the views expounded by Regis and Lavaure in 1893 with regard to delirium following operations in general, the source

of the intoxication being endogenous or exogenous.

Acute Dacryoadenitis.—Inman, House Surgeon, Royal London Ophthalmic Hospital (Reports, October, 1903), reports 10 cases of this affection observed at the hospital in two years, a rather extraordinary number, considering the experience of others; thus Arlt in his "Lehrbuch," 1853, says he has never seen a case; Powers asserts in 1886 that the indices of the Royal London Ophthalmic Hospital Reports make mention of only one case of abscess of the lacrymal gland. Hirschberg states that among 22,500 recorded cases of diseases of the cyc, he met with but one case of suppurative inflammation of the gland.

The cases of this disease described in literature divide themselves into two main groups: (1) Those in which the affection of the lacrymal gland is associated with mumps. The main features are: it is usually bilateral and suppuration does not occur. (2) Those in which there is no connection with mumps, the main features being that it is usually unilateral; suppuration may or may not occur. It is a disease of the

young, although it may occur at all ages. Of the writer's 10 cases—6 males, 4 females—the average was sixteen years, youngest three years, oldest thirty-seven years. The left side was more frequently attacked than the right; thus in this series, 9 out of 10. No cause can be assigned for this marked difference. The connection of this disease with mumps has been noted, though in this series of cases only one was so associated. The lacrymal sac was invariably healthy.

The symptoms are: beginning with a series of sensations of stiffness in the outer part of the upper lid, there is some pain and redness, with slight injection of the conjunctiva. The pain increases with the progress of the disease accompanied by marked cedema of the ocular conjunctiva on the outer side out of all proportion to the conjunctival inflammation accompanying it. The lacrymal gland shows distinct enlargement and induration; the vessels lying upon it are swollen and tortuous; there is moderate malaise and slight fever reaching 100° F. as the highest. As the disease progresses the eye becomes completely closed and the upper lid cannot be raised voluntarily, while eversion of the lid is extremely painful. The disease may be confounded with orbital cellulitis. This probably accounts in part for the rarity of recorded cases.

The outcome is favorable. The treatment is simple, consisting of hot fomentations with free incision to evacuate pus when such can be

detected.

#### OTOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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The Limits of Variation in the Depth of the Mastoid Antrum.—Philip D. Kerrison (Archives of Otology, June, 1903) gives some interesting results obtained from making sections of a large number of temporal bones to find out the maximum depth of the antrum to which one can proceed with safety. Politzer gives 15 mm. as a maximum depth, while Schwartze and Broca give 25 mm. and 29 mm., respectively. The author examined thirty bones to discover if any relationship exists between the length of the posterior canal wall and the depth of the antrum. The distance in millimetres between the spine of Henle externally and the inner border of the meatus was measured, then sections through the antrum were made and the distance between the antrum and the mastoid process was taken. In the thirty bones examined the length of the superior canal wall varied from 12 mm. to 18 mm. and in the same bones the depth of the antrum varied from 6 mm. to 15 mm. The deepest antrum measured 15 mm., this extreme depth

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occurred in the bonc in which the length of the posterior canal wall measured 18 mm. Emphasis is laid upon the fact that the depth of the antrum is invariably less than the length of the posterior canal wall and never exceeds 15 mm.

Broca directs that the antrum be opened in the centre of a square, the anterior border of which is 5 mm. behind the spine of Henle. This point is the thickest part of the mastoid process and naturally the antrum would lie at an unusual depth.

The author also calls attention to the location of the facial and the

semicircular canals.

Facial Paralysis.—Norton L. Wilson (American Medicine, vol. vii., No. 7). In addition to its comprehensive review of the subject, this paper contains material of interest to the otologist, both on account of questions of function of the nerve and its branches and of lesions in its eourse, either secondary to causative conditions in the middle ear or differentiated from them.

The so-called first branch of the facial nerve is the stapedius, supplying the muscle to the stapes; the so-called second branch is a twig to the pneumogastric which, apparently, comes off the facial trunk just above the chorda tympani. This, like the other filaments to the ganglion, is sensory, and undoubtedly goes to the geniculate ganglion, being a part of the pars intermedia. The chorda tympani, considered the last branch of the facial in the Fallopian canal, is nothing more nor less than a continuation of the pars intermedia, supplying the anterior two-thirds of the tongue with taste. There is, therefore, but one branch in the facial canal which actually comes directly from the nerve, namely, the stapedius, the other branches being all sensory and probably a part of the pars intermedia.

In a case of lesion external to the stylomastoid foramen, the paralysis of the facial muscles, including the orbicularis and frontalis, is not

associated with disturbances of the senses of taste and hearing.

If the lesion occurs in the lower half of the facial canal, there is, in addition to the facial paralysis, loss of the sense of taste in the anterior two-thirds of the tongue on the affected side and a diminished secretion of saliva, the lesion involving the chorda tympani and twig from the glossopharyngcal nerve.

If the lesion is in the upper half of the canal so that the stapedius is involved and not the ganglion, there is, in addition to the symptoms above named, an abnormal acuteness of hearing, for tones of high pitch especially, because the paralysis of the stapedius permits the unhindered contraction of the tensor tympani, and a correspondingly increased

tension of the sound transmitting apparatus of the middle ear.

Concomitant paralysis of the soft palate is usually attributed to involvement of the superficial petrosal, assuming that this nerve comes from the geniculate ganglion. In this opinion the writer does not concur, regarding these filaments as sensory and not motor, and that it is the fifth nerve which innervates the palate, and which is, therefore, the nerve involved when the palate is paralyzed. In support of this contention is the case of a man who fell a distance of eighteen feet, and was pieked up unconscious, bleeding from both ears. The hemorrhage from the ears continued for two days, and he was apparently totally deaf, both to sounds acrially conveyed and to the tuning-fork, by bone-con-

duction. The left side of the face was paralyzed, and there was complaint of tinnitus and vertigo. There was a fracture of the base of the skull involving both eighth nerves and the seventh nerve of the left side. There was no sense of taste in the anterior two-thirds of the tongue on the left side, and on this side, also, the salivary secretion was apparently diminished. The uvula and soft palate were normal. Contractility of the muscles of the left side of the face was lost for the faradic current, but was apparently increased for the galvanic current.

Were the geniculate ganglion involved and the general contention correct, the soft palate would have been affected, but in this case it

was normal.

Where the eause of a facial paralysis is of otitie origin, attention must be directed to the cause, and the importance of the electric reactions, both as symptoms and as prognostic indications, must be duly regarded. Electric changes soon develop in paralyzed muscles, and the reaction of degeneration, partial or complete, appears in four or five days after

the paralysis occurs.

Electricity should not be applied, except to ascertain the excitability of the muscles, until the end of the third week. One month after the paralysis has occurred, electricity and massage should be used regularly and systematically. If the muscles respond to faradism, that current should be used; if they do not, galvanism should be used, but only with the galvanometer, in order that the strength of the current may be known and gradually increased if necessary.

Einige Versuche ueber die Uebertragung von Schallschwingungen auf das Mittelohr.—Nagel and Samoyloff (Archiv für Physiologie, 1898; Archiv für Ohrenheilkunde, November, 1903) state that the graphie demonstration of the movements of the drumhead, in response to sound waves or the use of the membrane as a manometrie capsule for the same purpose, presuppose some approach to normal flexibility. This is attainable either through the use of fresh specimens or by the infiltration of the tissues of the membrane with substances which serve to conserve its mobility.

For the grosser forms of graphic demonstration, drumhcads thus conserved will give good service for a eonsiderable time, months or even years, and may be used also as manometric eapsules for demonstration of their movements by actuation of an illuminating gas current feeding a sensitive flame, but never so satisfactorily as the membrane of a freshly killed animal or the normal membrane *in situ* in the living

subject.

The latter method consists in making the external auditory canal a closed chamber by means of a stopper having two openings, one by which the illuminating gas enters the canal and the other by which it

passes on to the lighted gas jet.

Actuation of the drumhead by singing, speaking, or by communication of sounds conveyed through the bones of the head, are transmitted to the gas current in the external canal and made manifest in the movements of the sensitive flames, care being taken to guard the latter from the extraneous influence of sounds aerially conveyed.

In their experiments Nagel and Samoyloff have used, as a gas chamher, not the external canal, but the tympanic cavity of freshly killed animals and of the living subject. In the former instance the illuminating gas

was introduced by means of a fine trocar passed through the Eustaehian tube, while exit to the burner, a platinum tip with a minute opening, was afforded by a drillhole through the thin floor of the tympan and the insertion therein of a small rubber tube. In the living subject a tube with a T-shaped outer end was passed into the Eustachian tube, one end of the "T" connecting with the gas supply, and the other, by means of elastic tubing, with the burner.

Under these conditions sounds conveyed to the drumhead through the external canal and the vocalization of the subject of the experiment, even when only a light whispering voice was used, gave much more detailed representation in the flame than that afforded by the König

manometric eapsule with a rubber membrane.

Experiments were also made in reference to the question of craniotympanic sound transmission, but, although in themselves interesting, they seemed to have failed to negative the idea of the cranial passage of

sound waves direct to the internal ear.

A vibrating tuning-fork, the influence of which upon the flame when held opposite the external canal had been noted, was placed with its stem upon the skull and the character of the flame effect compared with that produced when the external ear was firmly closed, the reaction of

the flame, in the latter instance, being much increased.

That the term craniotympanic, as referred to the participation of the sound-transmitting mechanism of the middle ear in conveyance to the labyrinth of tones transmitted to the eranial bones is justifiable was shown by another experiment, in which, the vibrating tuning-fork having been placed upon the skull at the point previously found to give the greatest flame reaction, quieksilver or melted paraffin was poured into the external canal, effectively damping the movement of the drumhead. Under these circumstances the eraniotympanic reaction was entirely wanting, the sensitive flame showing no movement whatever. On removal of the quieksilver or paraffin the flame immediately responded to the tone of the vibrating tuning-fork.

### HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Measurements of Relative Humidity in Offices and Dwellinghouses in Winter.—An interesting proof of the statement that the air of heated houses in winter surpasses in aridity any climate in the world is given by G. A. LOVELAND (Engineering News, December 10, 1903, p. 925), who relates that in consequence of the evident effect of dry air on the furniture in the United States Weather Bureau Office in Lincoln, Nebraska, which is heated by steam radiators, a consecutive record of the relative humidity was made during the following winter. The obser-

vations, made by means of the sling psychrometer, were taken usually twice a day, but sometimes four or five times, and occasionally but once. They showed that during the whole winter the air was exceedingly dry. During the coldest month, February, with a mean temperature of 19.2° F. above zero, the average relative humidity of the office air was but 15.3 per cent. The extreme range was from 7 per cent. to 25 per cent., but only once was the relative humidity higher than 20 per cent., and only once did it fall below 10 per cent. In December, with a mean temperature of 22.6° F., the average relative humidity indoors was 18.6 per cent., and in January, which was the warmest month, with a mean outdoor temperature of 26.8° F., the indoor humidity was 21 per cent. The office temperature during the three months averaged slightly below 70° F. The mean relative humidity outdoors was 77.4 per cent. in December, 73.4 per cent. in January, 77.9 per cent. in February, and 76.2 per cent. for the three months, against but 18.3 per eent. indoors. These results led to further experimentation in a double house, the two halves of which were heated by furnaces of the same size, pattern, and make. The water-pan of each furnace had a capacity of twenty quarts. In one house the amount of water evaporated was determined each day at noon and was found to be but two quarts; in the other the pan was left empty for purposes of comparison. It was found that the difference in relative humidity in the two was so very slight (about 1 per cent.) that the value of the water-pan was not estab-After seventeen days' observation the amount evaporated daily was increased to five and nine-tenths quarts by placing pans of water in each of the registers of one house. This resulted in increasing the relative humidity of that house 2.4 per cent. over that of the other. Additional pans were then placed in the cold-air box, whereby the amount of water evaporated daily was increased to ten quarts, but even then the difference in humidity was but 2.2 per cent. Taking into account the probable rate of natural ventilation, it was reckoned that it would require from seventy to one hundred and fifty quarts of water, or possibly more, per day to maintain the relative humidity as high as it was outside, the difference between inside and outside temperatures being from 35° to 50° F., as is the case in winter in Nebraska. the first period of the experiment the outside and inside relative humidities were, respectively, 68.2 per cent. and 36.2 per cent.; in the second they were 73.8 per cent. and 35.8 per cent.; and in the third, 66.8 per eent. and 29.1 per cent. The average outside and inside temperatures during the three periods were 39.4° F. and 72.1° F., 39.3° F. and 70° F., and 33.3° F. and 69.9° F.

(By means of the "humidifier," which presents to the hot air issuing from a register a surface of wicking kept saturated with water, the relative humidity of the air of a room can be maintained at over 50 per cent., according to Dr. H. J. Barnes, of Boston, who brought it to public notice. In a large office building in Boston the air is maintained at about 50 per cent. relative humidity by means of steam injected into the hot air in the stock-room, from which the air is distributed to the various rooms. The amount of water thus vaporized in a ten-hour

workday is no less than 675 gallons.—C. H.)

Shellfish and Typhoid Fever.—It is the belief of Dr. J. T. C. NASH (Journal of State Medicine, December, 1903, p. 70) that scwage-con-

taminated shellfish have played a very large if not a leading part in the general incidence of typhoid fever in England. Prior to the advance in sanitary administration, the chief factors in the incidence of the disease were undoubtedly polluted water and infected milk, but to-day these sources have been so attacked that, as compared with fifty years ago, the relative amount of typhoid has diminished considerably. Yet during the past ten years no improvement, but, on the contrary, a tendency to increase, has been observed, in spite of all sanitary effort. No notable instance of epidemic water-borne typhoid has been observed since the Maidstone and Worthing outbreaks, and milk-borne typhoid has been more uncommon; but yet there appears to be an apparently irreducible minimum of typhoid, with an actual slight increase in prevalence. The reason for this is, in his opinion, that sufficient attention has not been given to the consideration of eleanliness of other foods than milk, for otherwise, the mouth being the portal of infection, localities provided with pure water would not have an undue amount of the disease. An infeeted water-supply eauses a widespread epidemic; an infected milk-supply produces the disease among the customers of the particular dairies involved; but when an outbreak occurs where both the water and the milk are above suspicion, there must be some other common source. Polluted soil may be expected to act as a vehicle of infection only by the surface soil becoming pulverized and blown about by the wind, so that it is deposited on articles of food or directly in the open mouth; but surface soil, owing to the action of direct sunlight, dryness, and the ordinary soil bacteria, is not a favorable habitat for the typhoid organism, which, however, finds more favorable condi-. tions in the deeper layers, where there are fewer saprophytes, more moisture, and less light. Yet it must be admitted that aerial infection from polluted surface soil is an oceasional factor. On the other hand, contaminated foods are obvious and most probable sources of infeetion, especially in the case of those which are obtained in polluted water, such as shellfish, water-eress, etc. He believes that a very considerable proportion of eases of typhoid in England is duc to sewage-contaminated shellfish, and in substantiation he asserts that out of 105 cases noticed in his district in 1902, he traced some connection with shellfish in at least 82. He cites the fact that at a well-known seaside resort (presumably Brighton) about 30 per cent. of the eases of typhoid that have occurred for some years past have been attributed to this eause, and that at another, where the disease was unduly prevalent in 1898 and 1899 and was attributed to polluted mussels, the stopping of the sale of the mussels the next year was followed by a marked diminution in the number of eases reported. Owing to the bringing about of diminished consumption of shellfish, on the one hand, and of better methods of laying and cooking and of greater care in obtaining supplies from purcr layings, on the other, a very decided diminution in the incidence of the disease has occurred in his own district. By careful inquiry, he estimates that rather less than more than 5 per cent. of the population of that district are eaters of shellfish; and working out for typhoid fever the standard ratios during 1902 per thousand persons in each section of the population, he calculates that for the entire population the attackrate was 3.28 per thousand; for the shellfish-eating section, reckoned as 5 per cent. of the population, it was 51.25; and for the remainder, only 0.75. Among the shellfish vendors and their employes, he ealculates the attack-rate at no less than 160 per thousand. Furthermore, the seasonal incidence of typhoid fever in the country generally is at its lowest in May and June, which months are the close season for English and French oysters. During these months, also, cockles and mussels are not in their prime, and hence are less eaten than at other times. In addition to necessary legislation concerning supervision of all shellfish layings and cultivation beds, he recommends for the diminution of the apparently irreducible minimum of typhoid fever the avoidance of all contact with shellfish, except such as are beyond suspicion of sewage pollution, the avoidance of uncooked vegetables which have been subjected to manurial pollution, the early removal to hospital of all cases of the disease, careful and constant attention to effective disposal of sewage and all forms of refuse, and general cleanliness of all food supplies, especially shellfish and watercress.

According to an editorial in the Journal of the American Medical Association of January 23, 1904, a careful investigation by the Health Board of Orange, N. J., of a recent increased prevalence of typhoid fever, exonerated the water-supply of the city as the cause thereof, and led to the conclusion that the outbreak was due to the consumption of oysters procured from infected beds.

Concerning Yellow Fever.—Dr. L. O. Howard (Supplement to Public Health Reports, November 13, 1903) observes that, although the actual localities in which the stegomyia fusciata has been found are comparatively small in number, both in the United States and in other parts of the world, we have sufficient facts on which to base a sound generalization, both as to probable actual occurrence and as to the regions in which the species will readily establish if once introduced. All the occurrence within the United States, except at Nashville, fall within the limits of what are known as the tropical and lower austral zones, which include practically all the southern United States which border on the Atlantie Ocean and the Gulf of Mexico, with the exception of those portions of Virginia, North Carolina, South Carolina, Georgia, and Alabama which constitute practically the foothills of the Appalachian chain, namely, Western Virginia and North Carolina, the extreme northwestern corner of South Carolina, the northern part of Georgia, and the extreme northeastern corner of Alabama. The lower austral zone includes also the western half of Tennessec, the western corner of Kentucky, the extreme southern tip of Illinois, the southeastern corner of Missouri, all of Arkansas except the northern portion, the southern portion of Indian Territory, Southern Arizona, some of Northern Arizona, and southern strips in Utah, Nevada, and California. In the greater part of this territory and where the climate is not too dry, the stegomyia fasciata probably exists; and in all the rest of this territory where the climate is not too dry, it will undoubtedly flourish if once introduced. We may expect to find it everywhere in the moist tropical zone, or, at all events, when introduced at any point within the low, moist tropics, it may be expected to establish itself. It is noted that the geographical distribution of the yellow fever mosquito corresponds rather well with that of the Texas cattle tick.

The French Yellow Fever Commission, composed of Marchoux, Salimbeni, and Simond, which has pursued the study of yellow fever at

Rio de Janeiro for more than a year, reports (Annales de l'Institut Pasteiur, November, 1903) that all the eonelusions of Reed and his associates have been eonfirmed in every particular. Otherwise, its work has been unproductive. Dr. G. Sanarelli (Il Policlinico, November 21, 1903), however, still opposes the idea that stegomyia is a necessary factor in spreading yellow fever, and asserts anew the importance of the part played by B. ieteroides.

In a communication to Surgeon-General Walter Wyman (Public Health Reports, January 15, 1904), under date of December 18, 1903, the members of Working Party No. 2, Dr. M. J. Rosenau, chairman, report that from their studies at Vera Cruz, Mexico, during the summer of 1903, they are unable to corroborate all the findings of Working Party No. 1, having found phases of the organism my.cococcidium stegomyiæ

in normal mosquitoes.

The fact that it has been proved beyond doubt that the female stegomyja fasciata serves as an intermediate host and conveys the poison of yellow fever to non-immunes has led the Louisiana State Board of Health to promulgate the following recommendations (Public Health Reports, February 5, 1904): 1. The patient shall be put under a bar and the room properly screened, and all mosquitoes destroyed. 2. The house shall at once be closed and fumigated with pyrethrum powder, 4 ounces to 1000 eubie feet. Intoxicated mosquitoes must be swept up and burned. In ease house is not occupied, sulphur should be used, 7 pounds to room, etc. Fumigation must be repeated every fourth day for three or four times. Commence all over with every new ease of fever. 3. Every house or outhouse shall be so fumigated for a distance of 100 yards in every direction from the infected house. Fumigation repeated every fourth day for three or four times. 4. Great eare to be exercised to prevent new mosquitoes from entering the infected room. When they do so, they must be killed and burned. 5. All eisterns iu infected area must be screened or coal-oiled. 6. All vessels containing water must be emptied; pools and ditches drained and eoal-oiled. 7. All drains, sinks, and privies are to be liberally sprinkled with eoal-oil every third day for a period of eighteen days. Repeat after every new ease.

## PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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A Note on Experimental Arterial Atheroma —Attempts have been made by several investigators to produce atheroma of the aorta in animals by intravenous injections of bacteria or bacterial toxins. In some eases the aorta was previously injured. Crocq has reported nega-

tive results, while Thérèse and Pernice were only able to produce very slight microscopic lesions in the wall of the aorta. Boinet and Romary have described small, raised areas in the aorta, which, on microscopic examination, had the characters of gelatiniform plaques. They believed these areas were the result of baeterial infection of the arterial wall. Josué has observed the formation of true calcareous plates after repeated injections of adrenalin. GILBERT and LION (Arch. dc méd. cxp. ct d'anat. path., 1904, T. xvi. p. 73) describe lesions in the aorta which they found in two rabbits after repeated intravenous inoculations of both living and killed cultures of a paracolon bacillus. In these experiments the artery did not receive any previous injury. One animal was allowed to live six months, the other ten months, after the primary inoculation. The middle coat of the aorta was the one affected, and the lesion consisted in a sclerocalcareous transformation. In another series of experiments the aorta was injured, and later cultures of typhoid bacilli were inoculated intravenously. After a few days the animals were killed. An acute aortitis was found at the site of trauma. The authors conclude that it is possible to produce atheroma of the aorta and acute aortitis in animals by intravenous inoculations of bacteria and bacterial toxins. This may take place with or without previous injury to the arterial wall.

Searlet Fever, Protozoan-like Bodies Found in Four Cases.— MALLORY (Journal of Medical Research; 1903, vol. x. p. 483) has found in four cases of scarlet fever certain bodies which in their morphology strongly suggest that they may be various stages in the developmental cycle of a protozoan. They occur in and between the epithchial cells of the epidermis and free in the superficial lymph vessels and spaces of the corium. The great majority of the bodies vary from 2 to 7 mierons in diameter, and stain delicately but sharply with methylenc blue. They form a series of bodies, including the formation of definite rosettes with numerous segments, which are closely analogous to the series seen in the asexual development (schizogonia) of the malarial parasite, but, in addition, there are certain coarsely reticulated forms which may represent stages in sporogonia, or be due to degeneration of other forms. The bodies were not found in the blood, lymph nodes, or any of the internal organs. The possibility of these bodies being artefacts or degenerations can be effectually excluded. If they are protozoa they must have some eausal relation to searlet fever, for were they normal or occasional inhabitants of the skin, their presence could hardly have been overlooked in the extensive work which has been done on the skin. Though the author believes that these bodies are protozoa and have an etiological relationship to searlet fever, he does not claim that such a relationship has been absolutely proven. He proposes the name of "eyclaster scarlatinalis" for the organism.

Tuberculosis of the Tonsils in Children.—The belief has steadily been gaining ground that the tonsils are one of the most important channels by which the tuberele bacillus enters the system during childhood. A comparatively large number of cases in which tuberele bacilli or tubereles could be demonstrated in the tonsils of adults have been recorded, but only a few observers, especially Friedmann and Latham, have confined their attention to the study of the tonsils in children. Kingsford (Lancet, 1904, vol. i. p. 89) has examined the tonsils of seventeen

children under five years of age, which at autopsy showed tuberculous lesions in various parts of the body. Tuberculosis of the tonsils could be demonstrated microscopically in seven of these eases, but in only one was there any evidence that the tonsillar infection was primary. In the other cases the infection probably took place by means of the blood stream or expectorated sputum. The author concludes that though tuberculosis of the tonsils is fairly common, the process is rarely primary in the tonsils. If the tonsils are tuberculous the cervical glands are also affected, but it may happen that the infection enters the body through the tonsils and reaches the cervical glands without leaving a demonstrable lesion in the tonsils themselves.

The Pathological Anatomy of "Paratyphoid Fever:" a Fatal Case with Bacteriological Findings.-Wells and Scott (Journal of Infectious Diseases, 1904, vol. i. p. 72) have collected the pathological and bacteriological reports of four fatal cases of paratyphoid They describe in detail the history, bacteriology, and pathological findings of a fifth case. The case was one simulating typhoid fever, but giving negative Widal reactions throughout the course. The spleen was palpable, rose spots were present over the abdomen, and twice blood was passed in the stools. There was absence of depression, little or no delirium, and a relatively high pulse rate. At autopsy the general pathological picture was that of an acute infection. In the ileum, a short distance above the ileocæcal valve, an extensive ragged ulceration was found; the ulcers bore no relation to the lymphatic apparatus and appeared entirely dissimilar to the ulceration of typhoid fever, inasmuch as they were quite superficial and showed lack of infiltration. They resembled much more the ulcers of dysentery. There was no swelling either of the mesenteric or retroperitoneal lymph nodes. In sections the ulcers in the ileum looked entirely different from typhoid ulcers, particularly in the absence of infiltration and hyperplasia of the lymphoid follicles. The mesenteric lymph glands also showed total absence of congestion or lymphoid swelling of the lymph follicles and sinuses. A few foci of neerosis were seen in the liver. They were noticeable for their lack of endothelial cells. The spleen showed eongestion with the presence of large endothelial cells containing golden-brown pigment. Cultures from the spleen and kidney gave a pure growth of paratyphoid bacilli. With the serum of a rabbit immunized against Buxton's paratyphoid bacillus, they agglutinated in dilutions of 1: 40,000. The serum did not react toward typhoid or colon bacilli. The authors conclude that paratyphoid infections are accompanied by changes quite different from those of typhoid fever. The intestinal lesions are variable, and there is little anatomically to differentiate this type of infections from other septicæmias.

Influence of Splenectomy on the Leukocytes of the Blood of the Dog.—Nicolas and Dumoulin (Jour. de phys. et de path. gén., 1903, T. v. p. 1073) conclude, from a study of the blood in two splenectomized dogs, that after splenectomy there is an increase in the number of white blood cells, and that this increase persists for some time after the operation, but eventually, perhaps after months, returns to the normal. There is an immediate diminution in the number of leukocytes, followed by a transient elevation of these cells. This finally gives place to a marked

and persistent decrease in the relative number of lymphocytes. The authors believe that this observation is important, inasmuch as it suggests that the spleen plays some part in the genesis of the lymphocytes. The polymorphonuclear leukocytes show a slight variation and are usually relatively increased. A marked cosinophilia occurred in one of the two dogs.

Changes in the Power of Absorption of the Animal Peritoneum Brought about by Intraperitoneal Injections of Adrenalin.-It is well known that the application of adrenalin to mucous surfaces causes anæmia, owing to the contraction of the capillaries. Exner (Zeitschrift für Heilkunde, 1903, Bd. xxiv. p. 302), applying this principle to serous surfaces, experimented with adrenalin to study its effect when, injected intrapcritoneally, upon the absorbing power of the peritoncum. Guinea-pigs and rabbits received intraperitoneal injections of adrenalin. Subsequently, when stryclinine, potassium cyanide, physostigmine, and indigo were given into the peritoneum, the onset of toxic symptoms from these drugs or their absorption was much delayed over the control animals. With potassium iodide, the time required for its appearance in the urine was the same in normal animals and animals which had received adrenalin intraperitoneally. To determine whether the adrenalin injections affected the absorption through the bloodvessels or lymphatics, a finc emulsion of paraffin in gum arabic was used. The absorption of this substance was much retarded by previous intraperitoneal injections of adrenalin. By staining the diaphragm with silver nitrate, the structures described as stomata appeared less numerous in the adrenalin animals than in the normal animals. It was, therefore, thought that absorption through the lymphatics alone was retarded by Adrenalin injections had a very marked retarding effect upon the extension of bacteria from the peritoneum into the circulating blood.

From the results of these experiments, the author suggests that in operations for peritonitis a very material benefit might be derived by previously injecting adrenalin into the peritoneal cavity. By this procedure it is possible that the absorption of bacterial toxins from the peritoneum might be lessened during the manipulation of the intestines at operation.

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